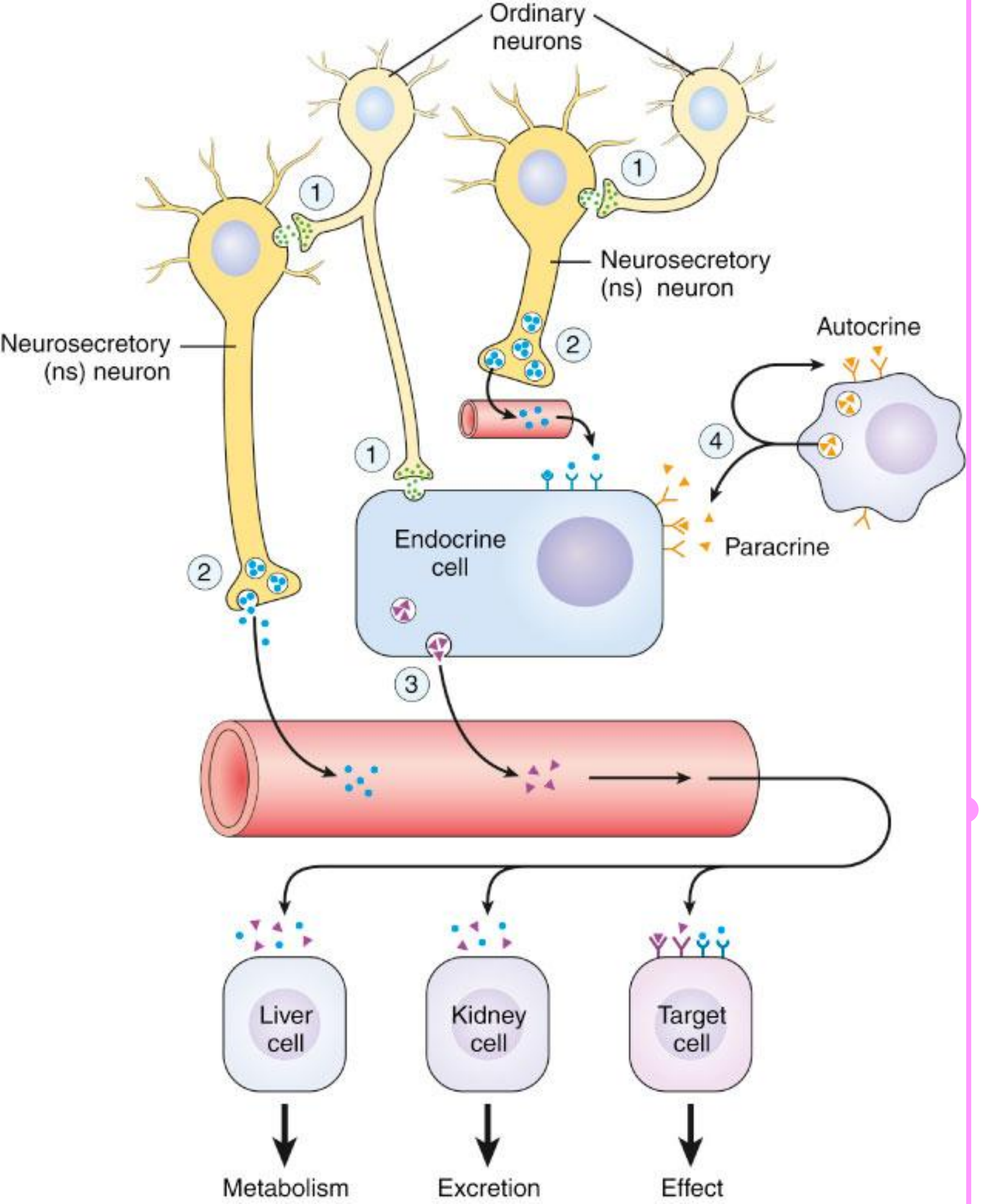
Hormones in animals and humans

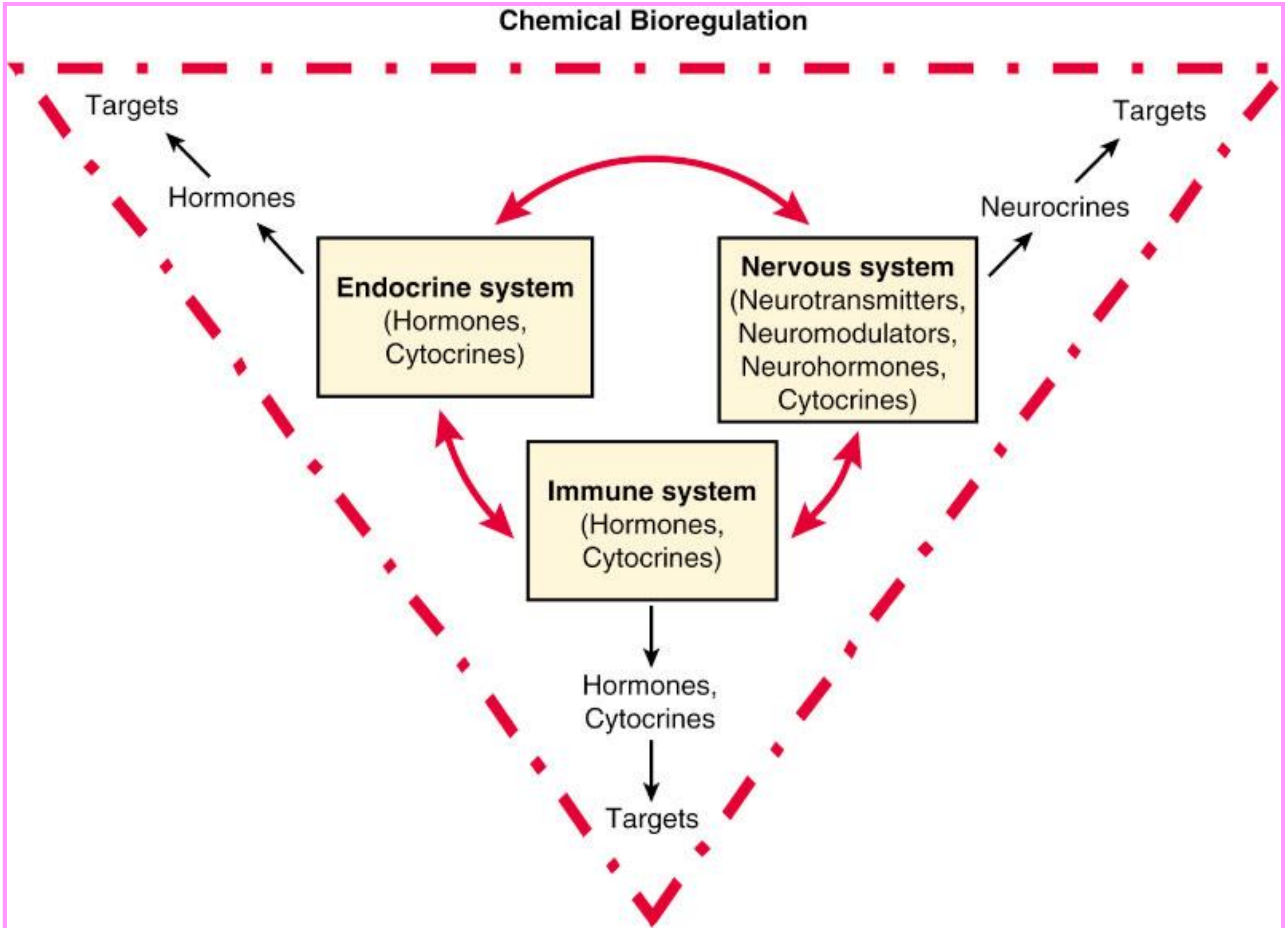


Categoreies of Bioregulators

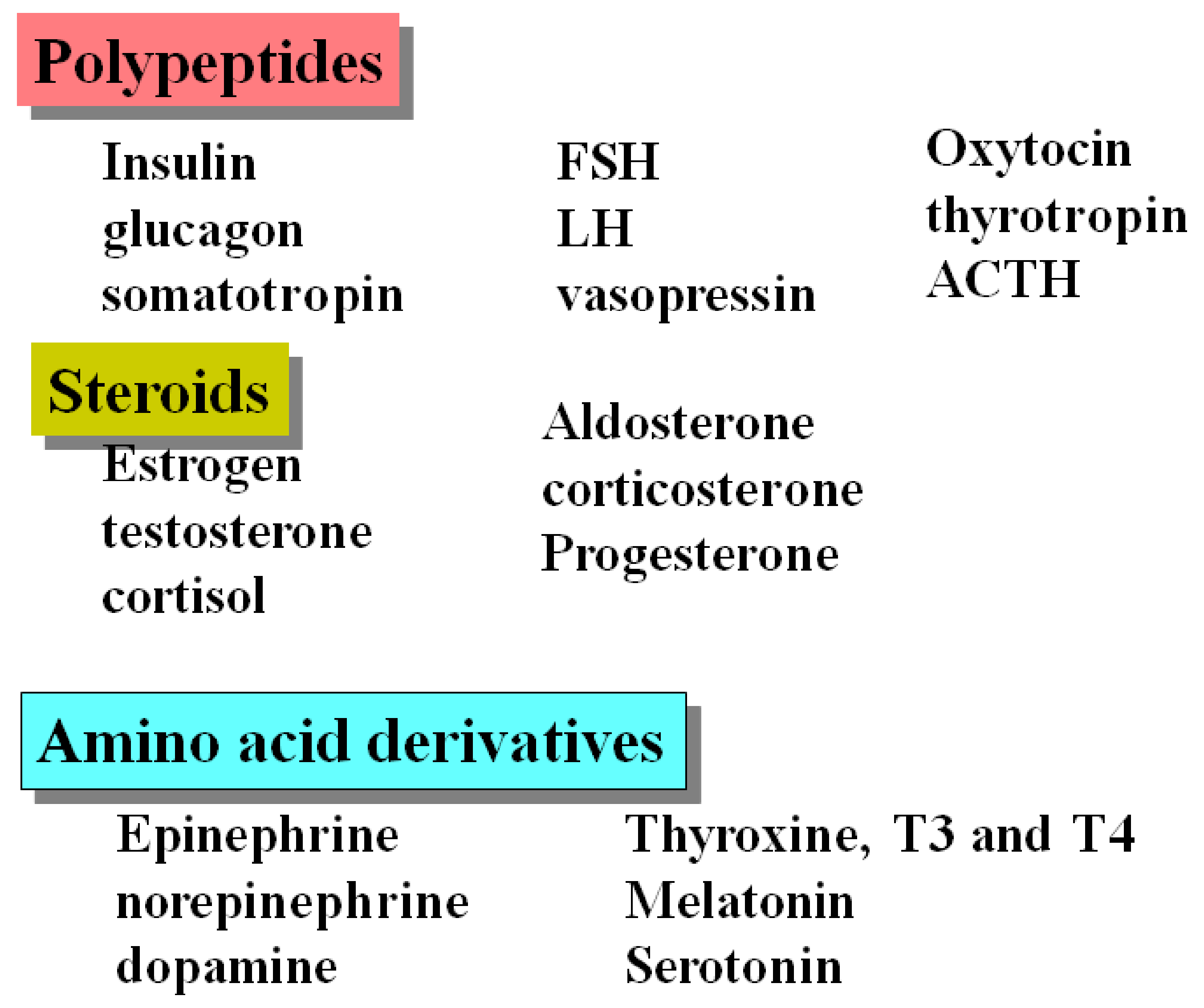
1. Neurocrines, including neurotransmitters or neuromodulators
2. Autocrine/paracrine regulators
3. **Neurohormones**
4. **Hormones**
5. **Ectohormones** (semiochemicals)

The liver and kidney serve as major sites for the metabolism and excretion of bioregulators.

Chemical Bioregulation



Hormones types



Polypeptides

Insulin
glucagon
somatotropin

FSH
LH
vasopressin

Oxytocin
thyrotropin
ACTH

Steroids

Estrogen
testosterone
cortisol

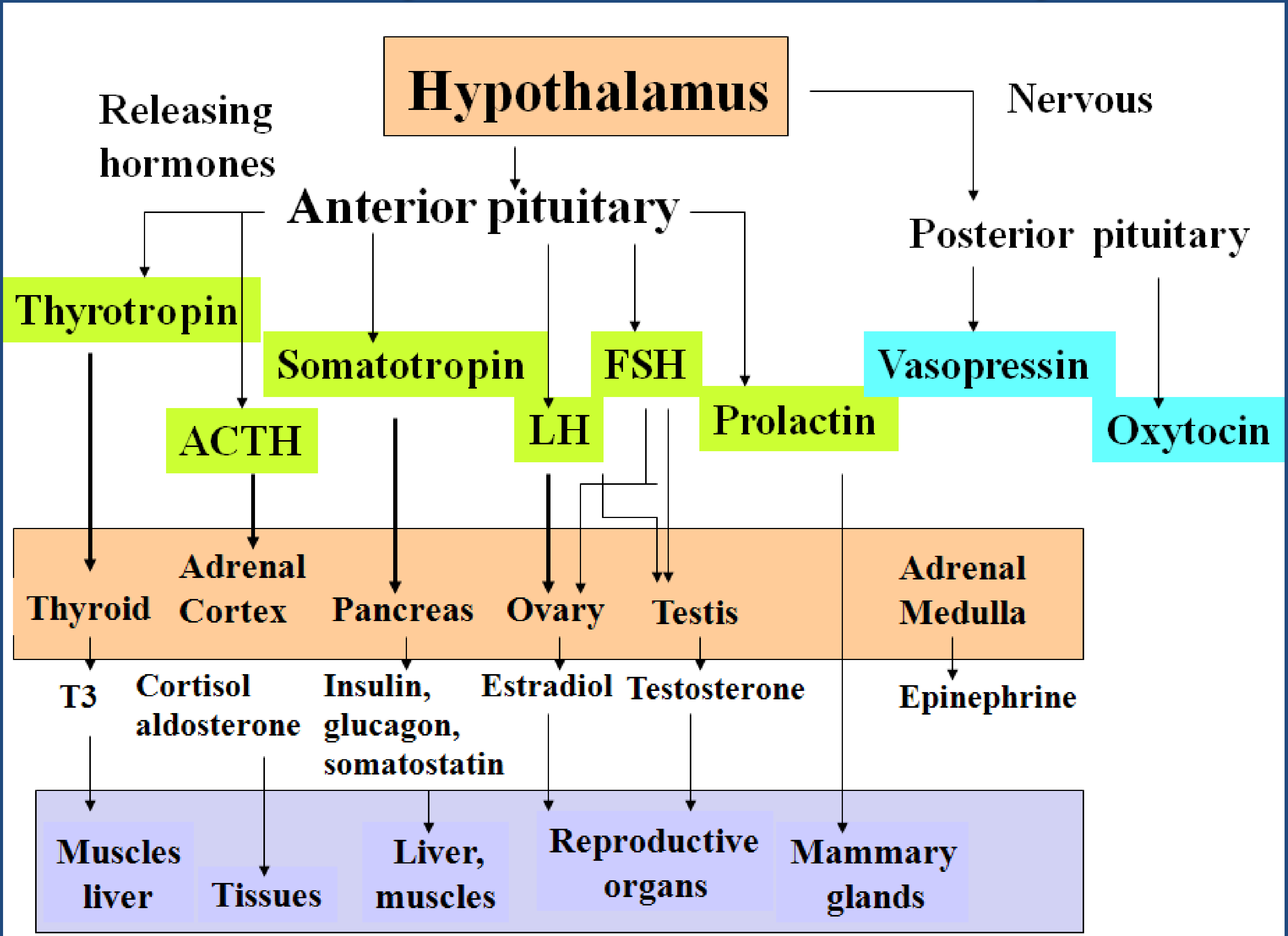
Aldosterone
corticosterone
Progesterone

Amino acid derivatives

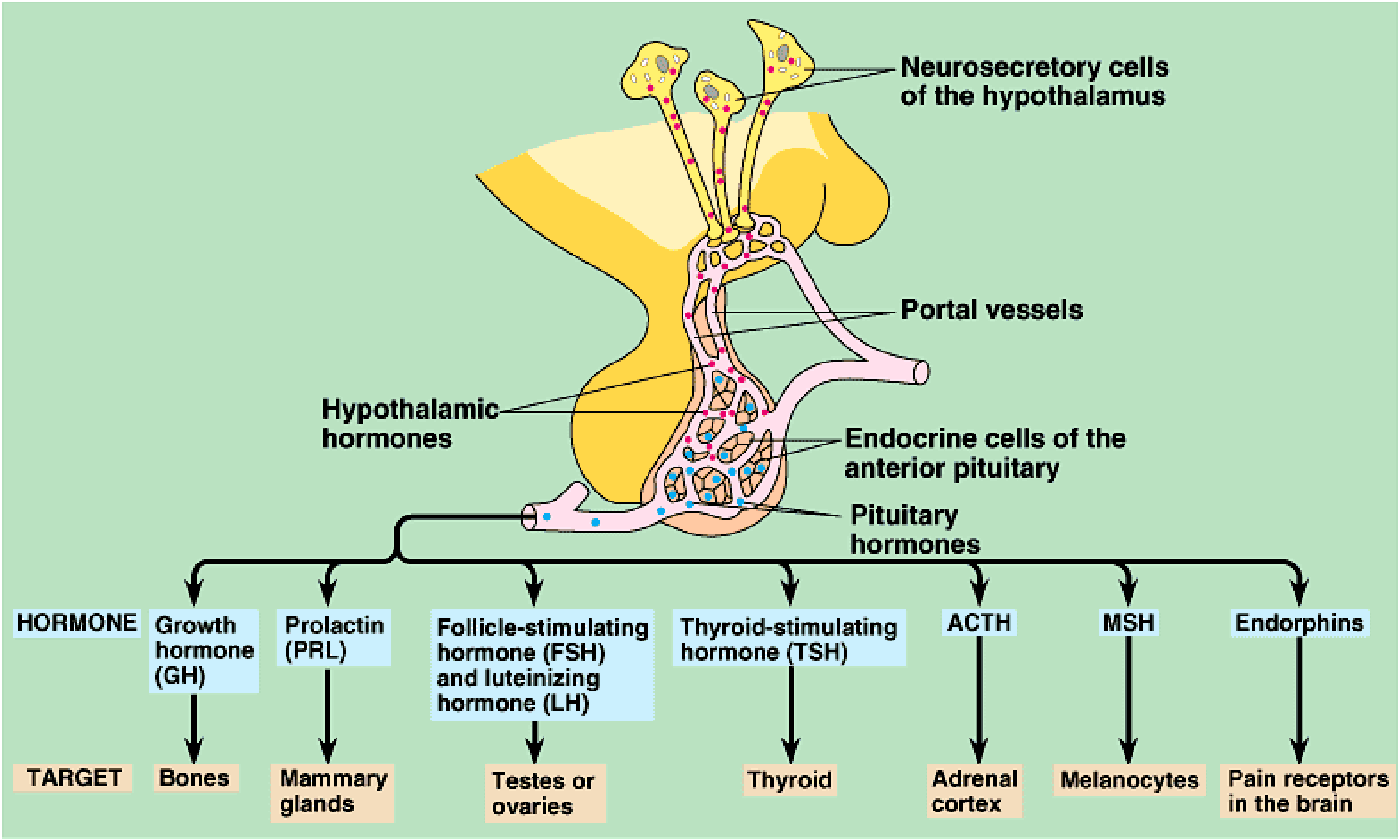
Epinephrine
norepinephrine
dopamine

Thyroxine, T3 and T4
Melatonin
Serotonin

Hierarchy of endocrine system

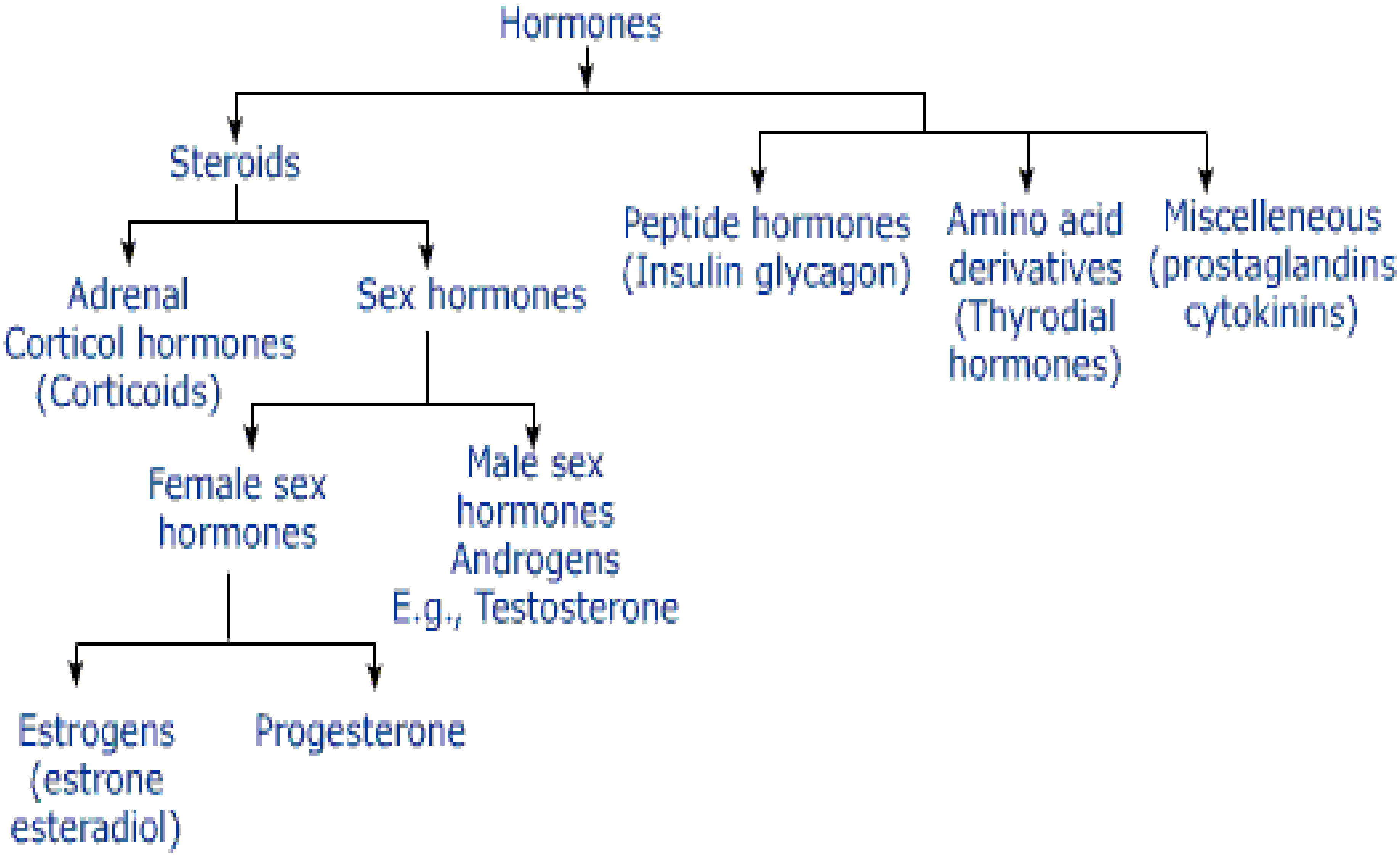


Tropic hormones


Neurosecretory cells of the hypothalamus
Portal vessels
Hypothalamic hormones
Endocrine cells of the anterior pituitary
Pituitary hormones

HORMONE	Growth hormone (GH)	Prolactin (PRL)	Follicle-stimulating hormone (FSH) and luteinizing hormone (LH)	Thyroid-stimulating hormone (TSH)	ACTH	MSH	Endorphins
TARGET	Bones	Mammary glands	Testes or ovaries	Thyroid	Adrenal cortex	Melanocytes	Pain receptors in the brain

(b) The anterior pituitary



- Hormones
  - Steroids
    - Adrenal Corticol hormones (Corticoids)
    - Sex hormones
      - Female sex hormones
        - Estrogens (estrone esteradiol)
        - Progesterone
      - Male sex hormones Androgens E.g., Testosterone
  - Peptide hormones (Insulin glycagon)
  - Amino acid derivatives (Thyrodial hormones)
  - Miscelleneous (prostaglandins cytokinins)

Hormone classes

GROUP –I

Types- steroids hormones

Solubility – Lipophilic

Transport Proteins- Yes

Plasma half life- long

Receptor- Intracellular

Mediator- Receptor- Hormone complex

GROUP –II

Types- Polypeptides, proteins, glycoproteins, catecholamine hormones

Solubility – Hydrophilic

Transport Proteins- No

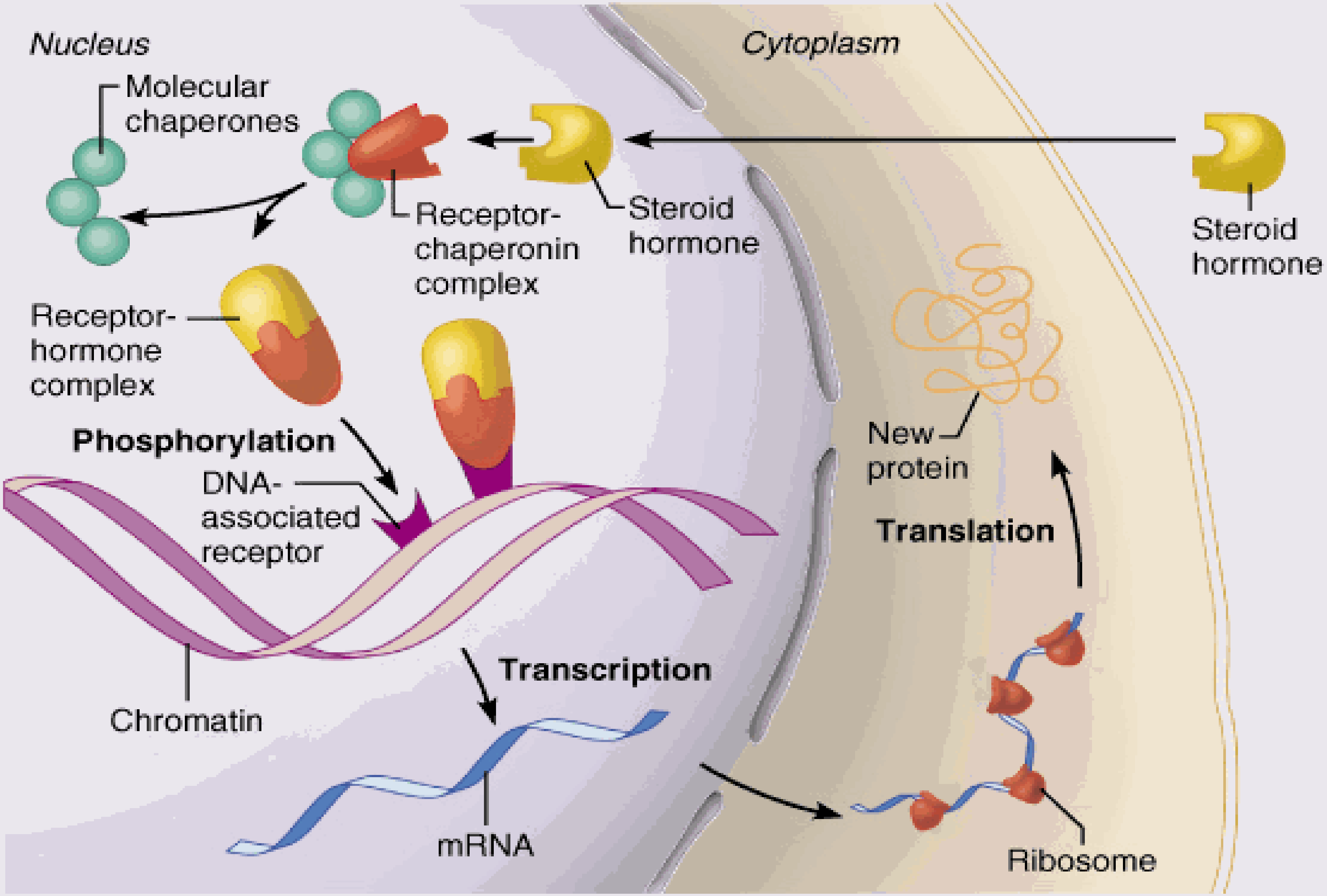
Plasma half life- Short

Receptor- Plasma membrane

Mediator- cAMP, cGMP, Calcium and phosphatidylinostinol.

- **Step-by-step**

1. Diffuse through the membrane
2. Binds & activates intracellular receptor.
3. Steroid-Receptor complex binds to DNA receptor protein
4. Activates a gene.
5. Gene transcribed into messenger RNA.
6. mRNA goes to the ribosomes
7. Translate mRNA into protein.



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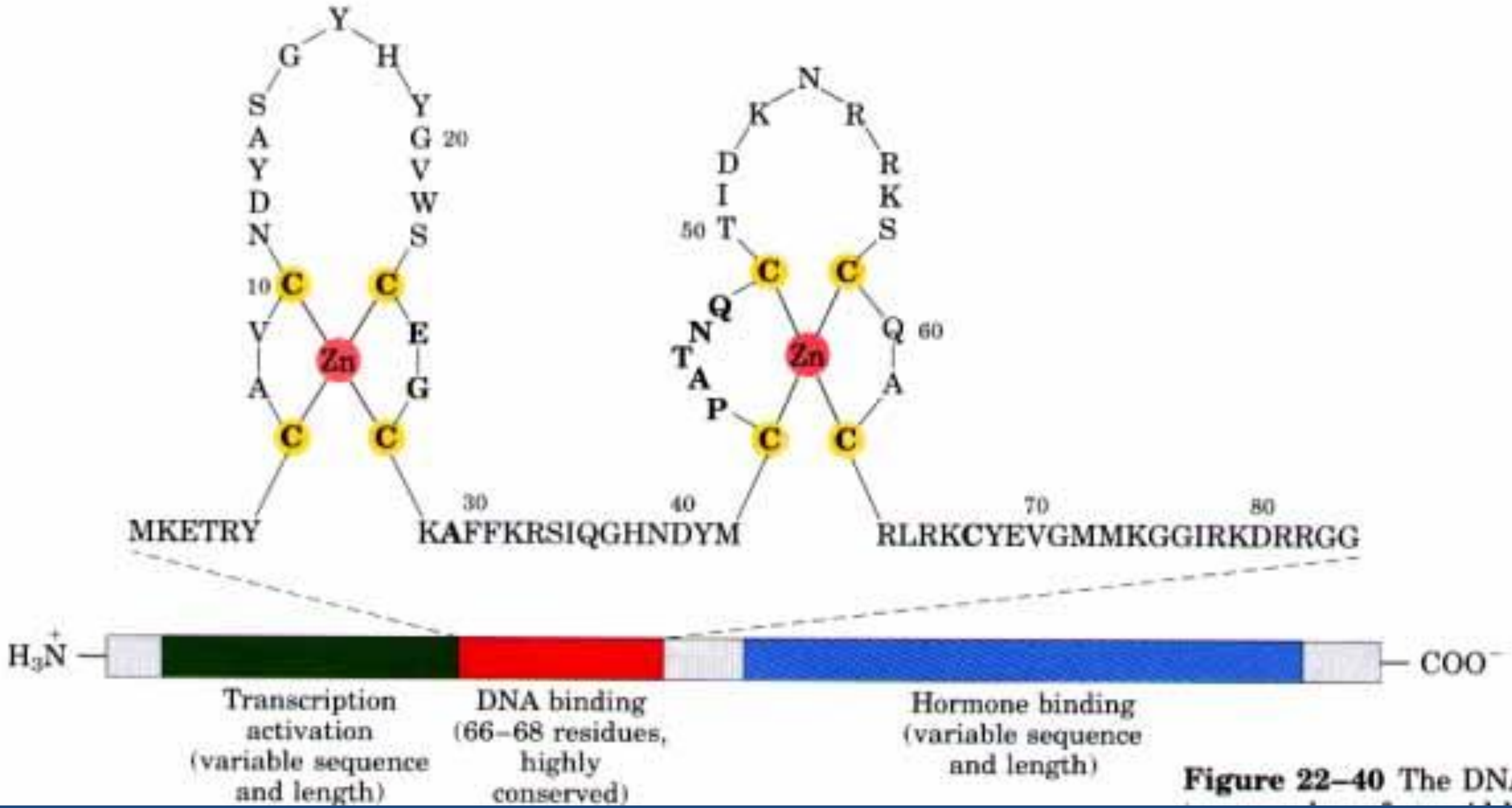

Y
G
H
S
Y
A
G 20
Y
V
D
W
N
S
10 C
C
V
E
Zn
A
G
C
C
N
K
R
D
R
I
K
50 T
S
C
C
Q
N
Q 60
T
Zn
A
A
P
C
C
30
40
70
80
MKETRY
KAFFKRSIQGHNDYM
RLRKCYEVGMMKGGIRKDRRGG
$H_3\overset{+}{N}$
COO⁻
Transcription activation (variable sequence and length)
DNA binding (66–68 residues, highly conserved)
Hormone binding (variable sequence and length)

Figure 22–40 The DNA

Hormone classes

GROUP –I

Types- steroids hormones

Solubility – Lipophilic

Transport Proteins- Yes

Plasma half life- long

Receptor- Intracellular

Mediator- Receptor- Hormone complex

GROUP –II

Types- Polypeptides, proteins, glycoproteins, catecholamine hormones

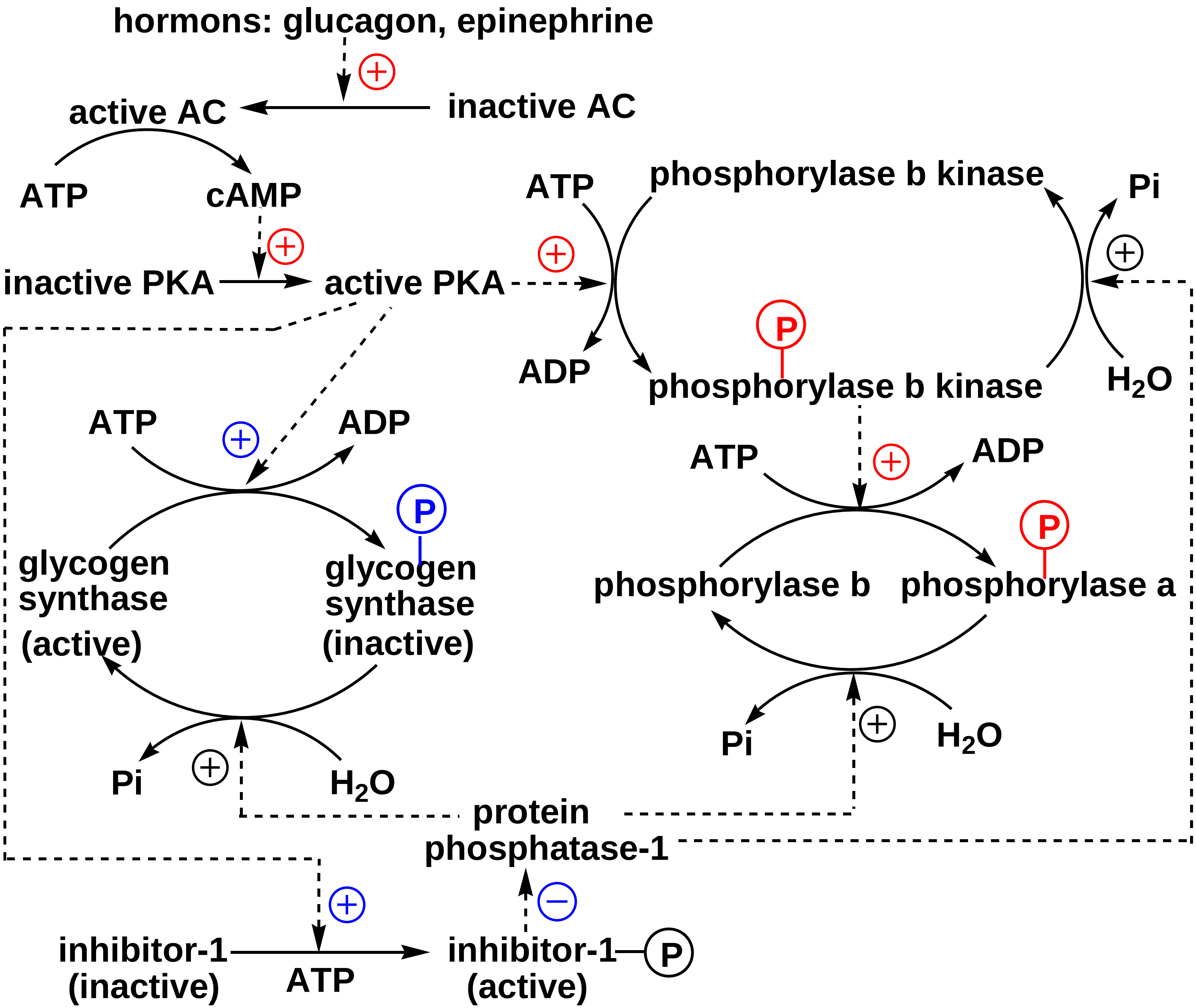
Solubility – Hydrophilic

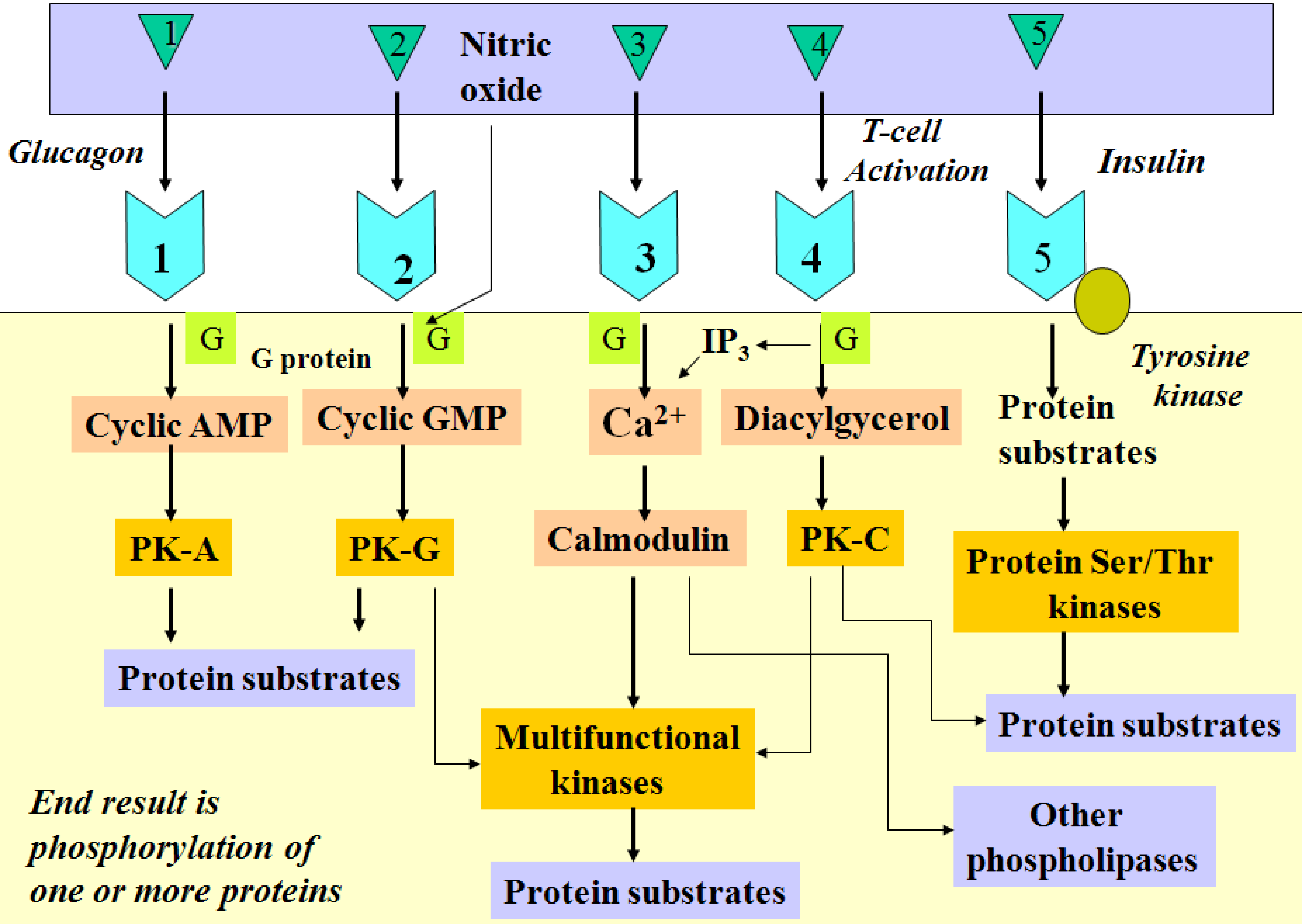
Transport Proteins- No

Plasma half life- Short

Receptor- Plasma membrane

Mediator- cAMP, cGMP, Calcium and phosphatidylinostinol.


hormons: glucagon, epinephrine
+
active AC
inactive AC
ATP
cAMP
+
inactive PKA
active PKA
+
ATP
phosphorylase b kinase
Pi
+
ADP
P
phosphorylase b kinase
H_2O
ATP
+
ADP
P
glycogen synthase (active)
glycogen synthase (inactive)
ATP
+
ADP
P
phosphorylase b
phosphorylase a
Pi
+
H_2O
Pi
+
H_2O
protein phosphatase-1
+
−
inhibitor-1 (inactive)
ATP
inhibitor-1 (active)
P



1 2 3 4 5

Nitric oxide

Glucagon

T-cell Activation

Insulin

1 2 3 4 5

G

G protein

G

G

IP_3

G

Cyclic AMP

Cyclic GMP

Ca^{2+}

Diacylgycerol

Protein substrates

Tyrosine kinase

PK-A

PK-G

Calmodulin

PK-C

Protein Ser/Thr kinases

Protein substrates

Multifunctional kinases

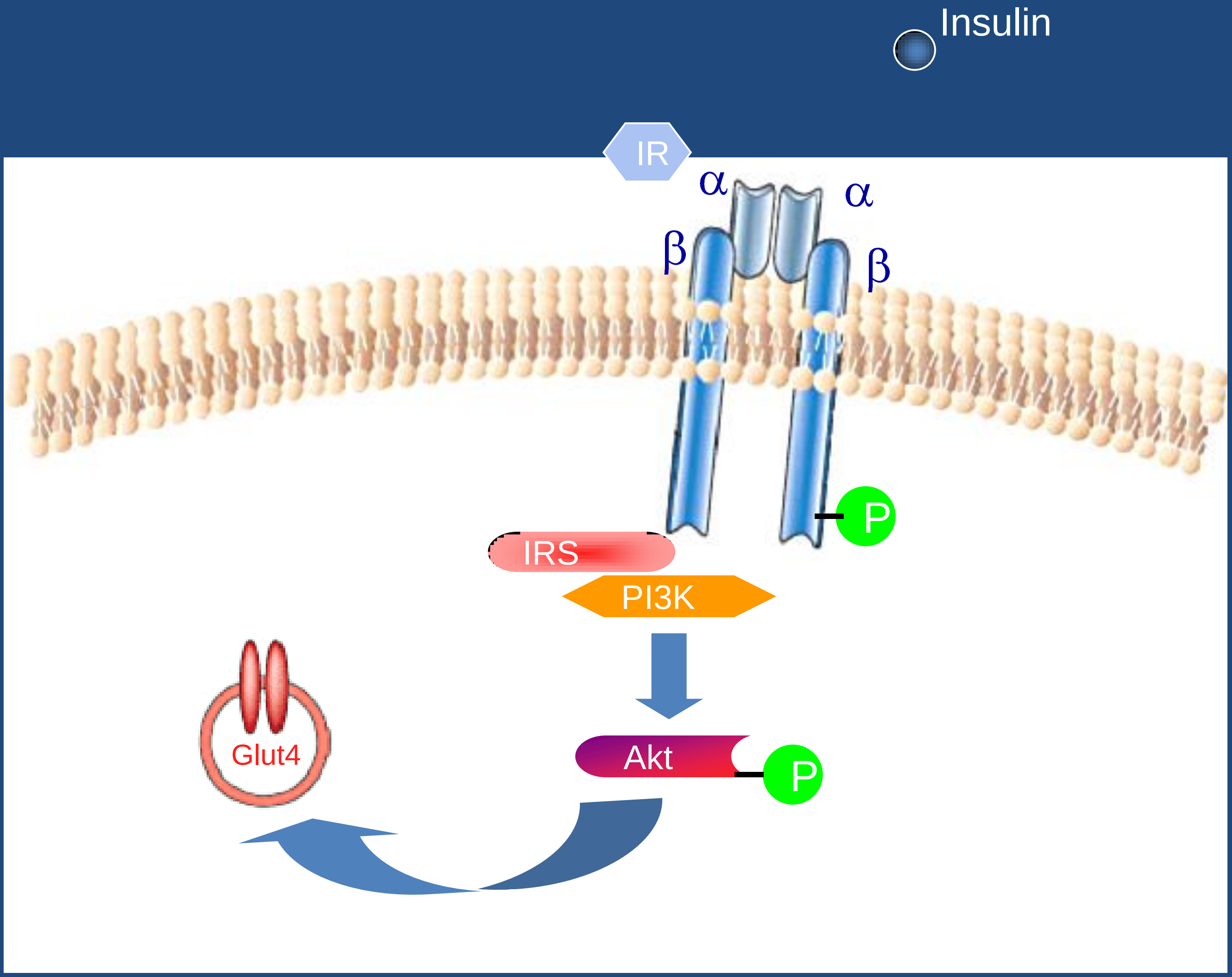
Protein substrates

Other phospholipases

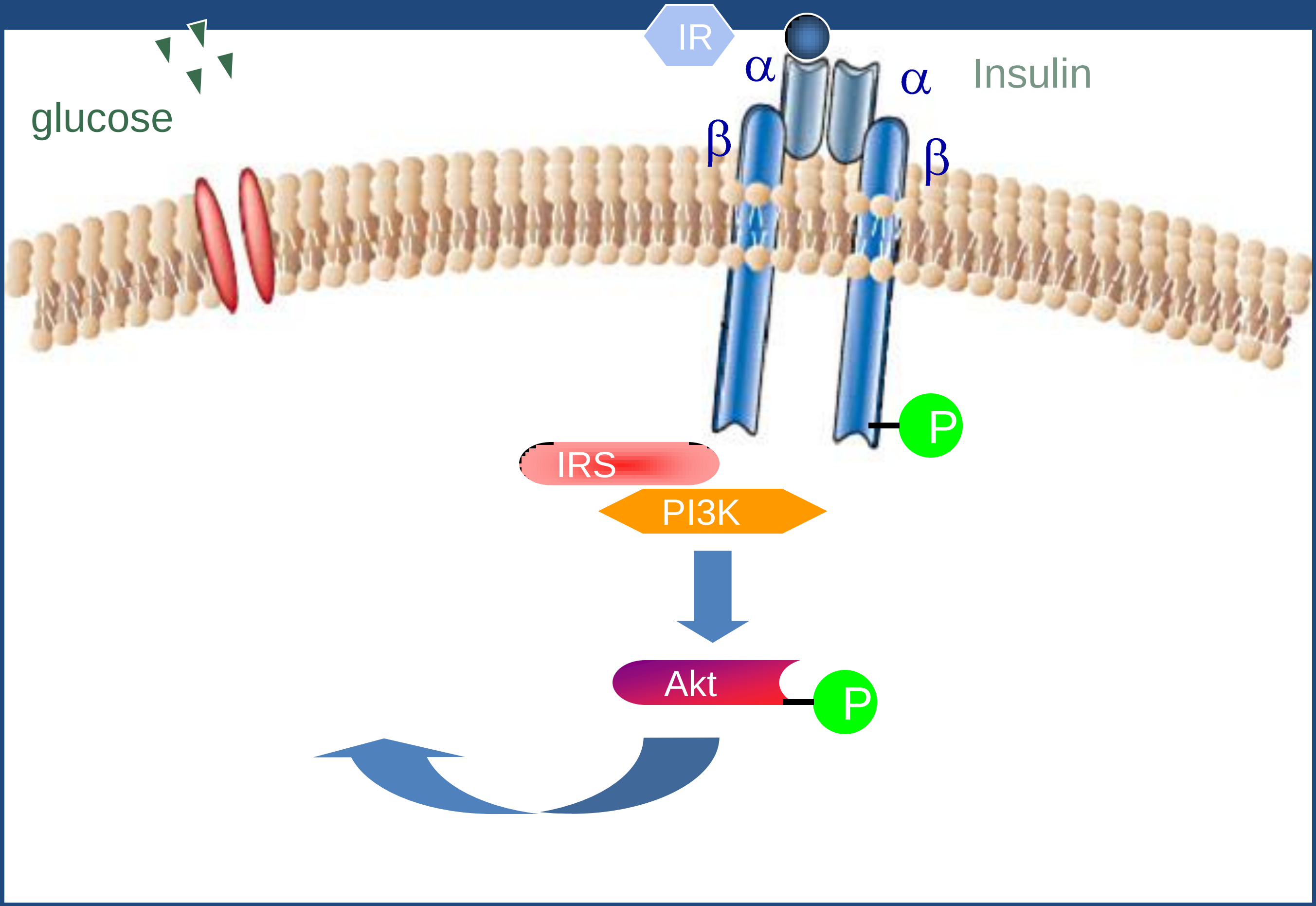
Protein substrates

End result is phosphorylation of one or more proteins

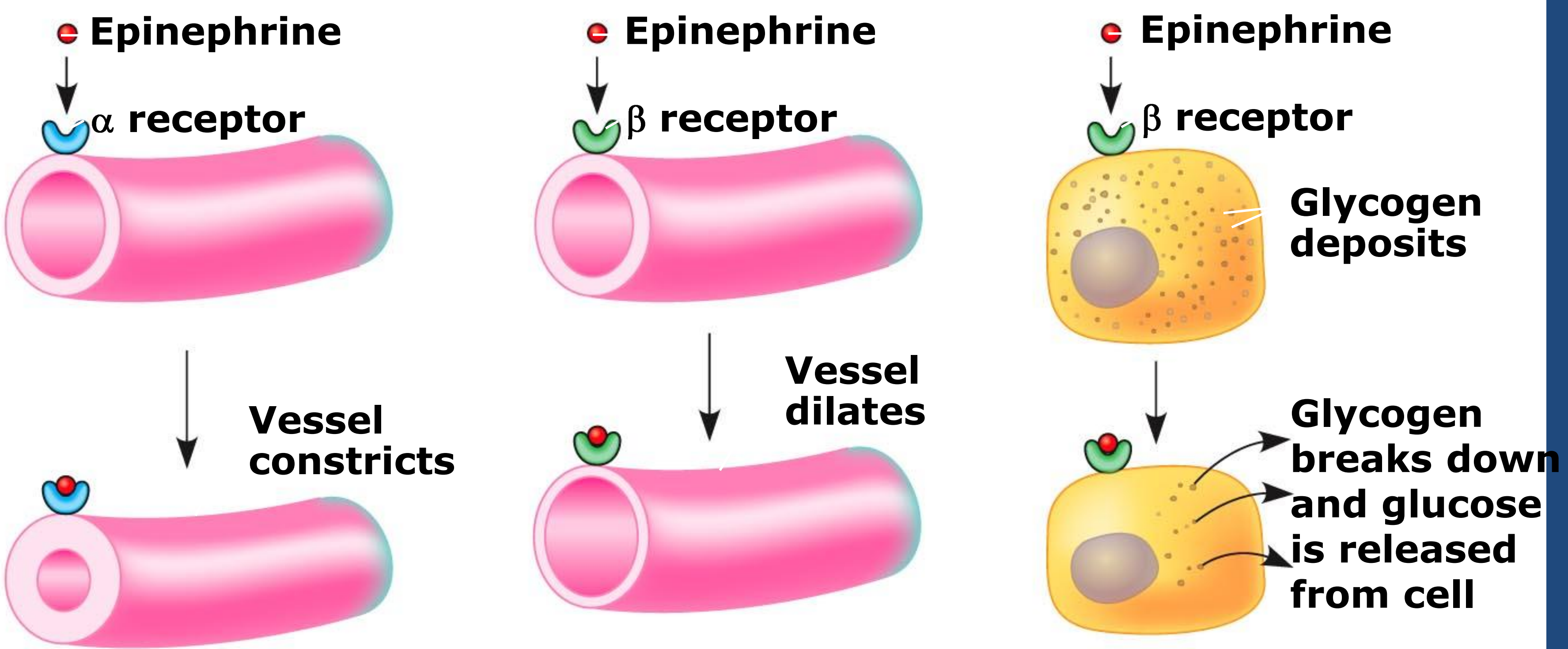
Insulin-mediated glucose transport signaling pathway



Insulin-mediated glucose transport signaling pathway



Different receptors → different cell responses



(a) Intestinal blood vessel

(b) Skeletal muscle blood vessel

(c) Liver cell

Different intracellular proteins → different cell responses

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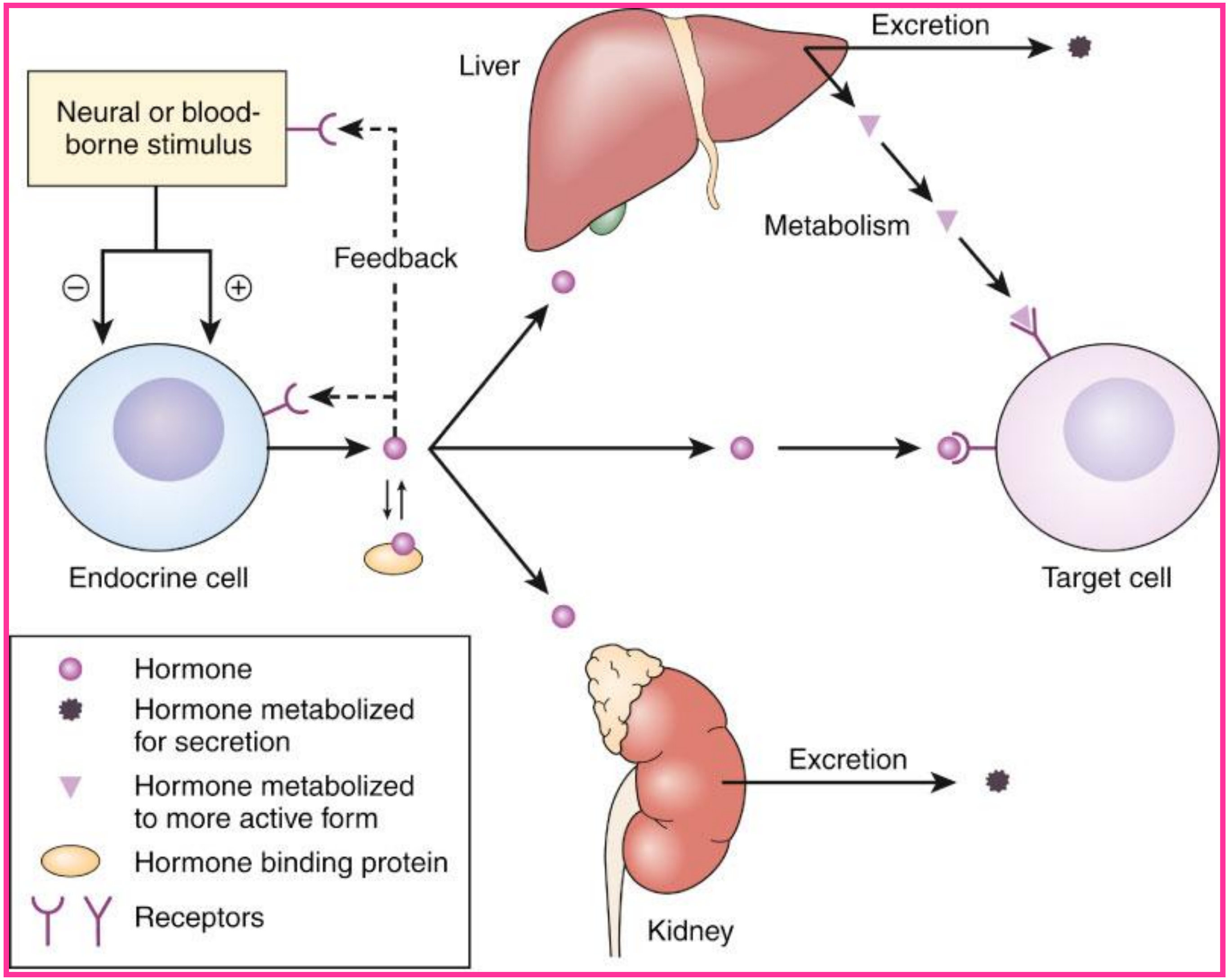
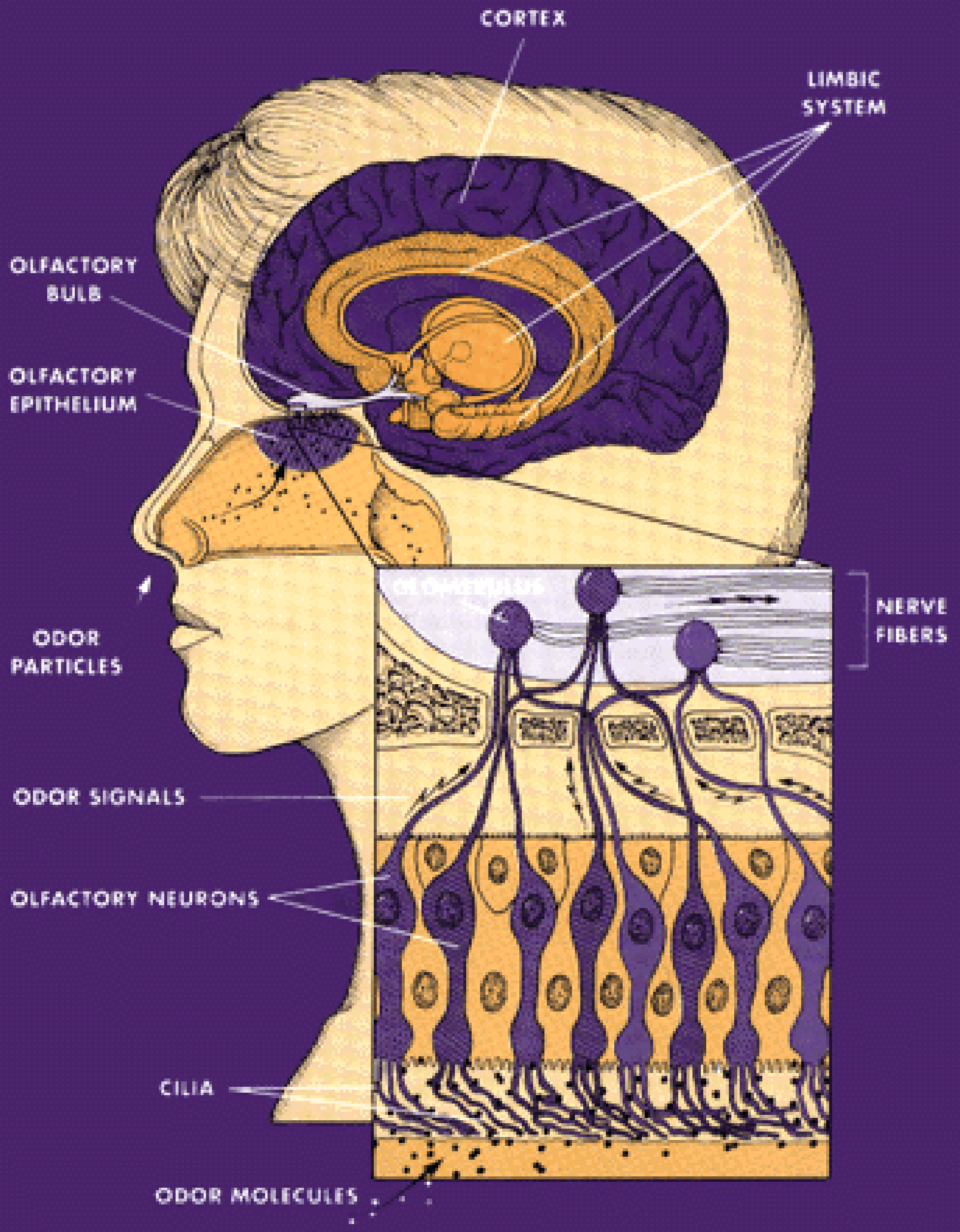
Life History of a Hormone


Neural or blood-borne stimulus
⊖
⊕
Feedback
Endocrine cell
Liver
Excretion
Metabolism
Target cell
Excretion
Kidney
● Hormone
✹ Hormone metabolized for secretion
▼ Hormone metabolized to more active form
⬭ Hormone binding protein
Y Y Receptors

Liver and kidney are major sites of hormone metabolism and excretion

The Olfactory System

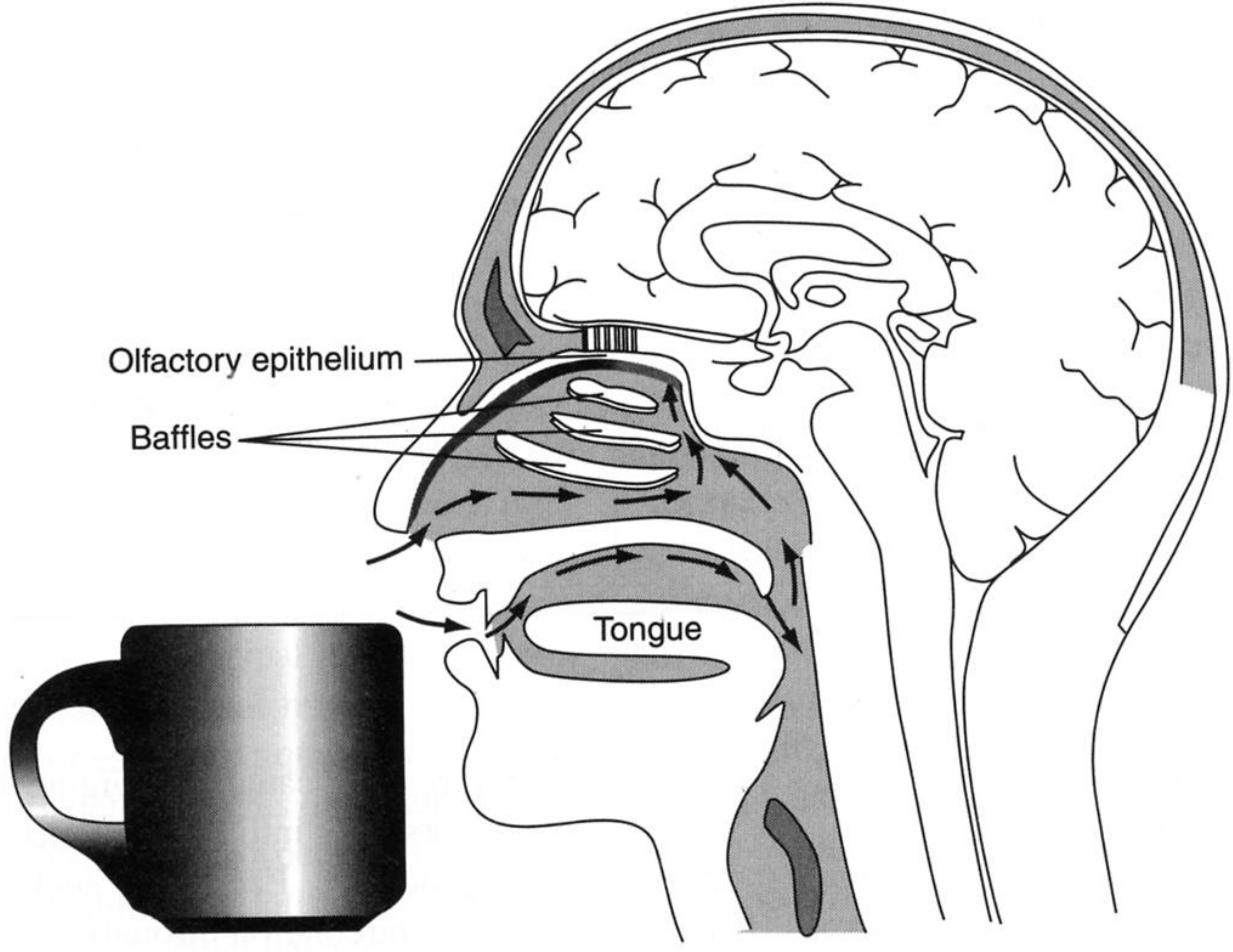


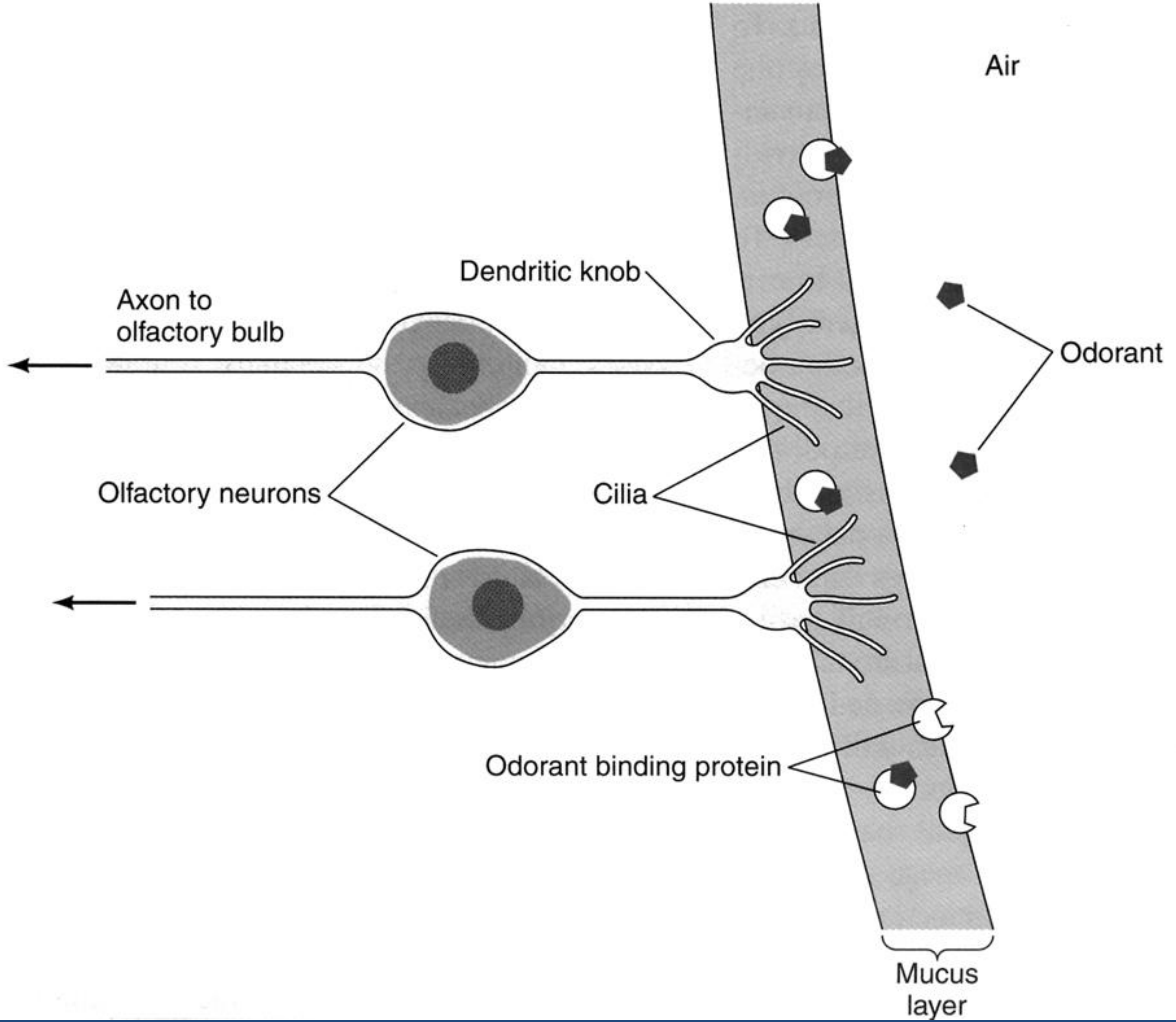
Olfactory System

Chemical sensing system with receptor organs in the nasal passages

Receptors synapse directly into the brain; heavy connections with the limbic system

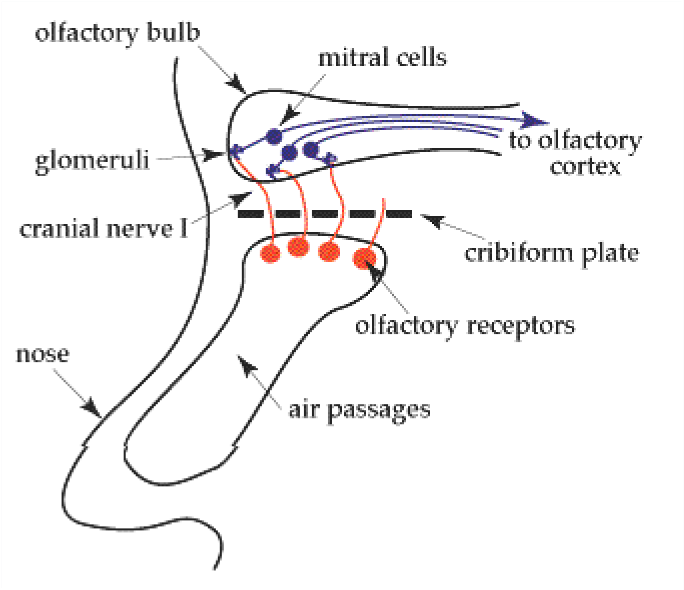
Different from other sensory systems in many ways


Olfactory epithelium
Baffles
Tongue

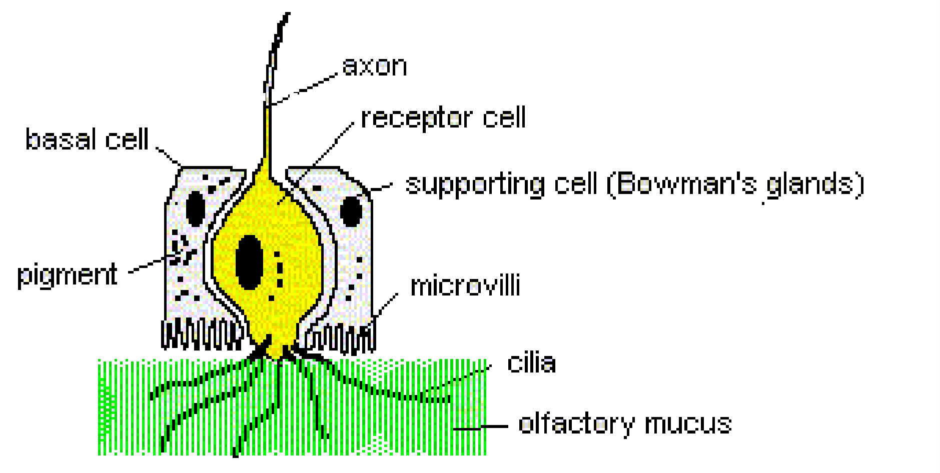

Air
Dendritic knob
Axon to olfactory bulb
Odorant
Olfactory neurons
Cilia
Odorant binding protein
Mucus layer

Olfactory System: Peripheral Structure

Olfactory receptors are located on the olfactory (or nasal) epithelium. The epithelium hangs down from the roof of the nasal sinus. The epithelium contains olfactory receptor cells and supporting cells.



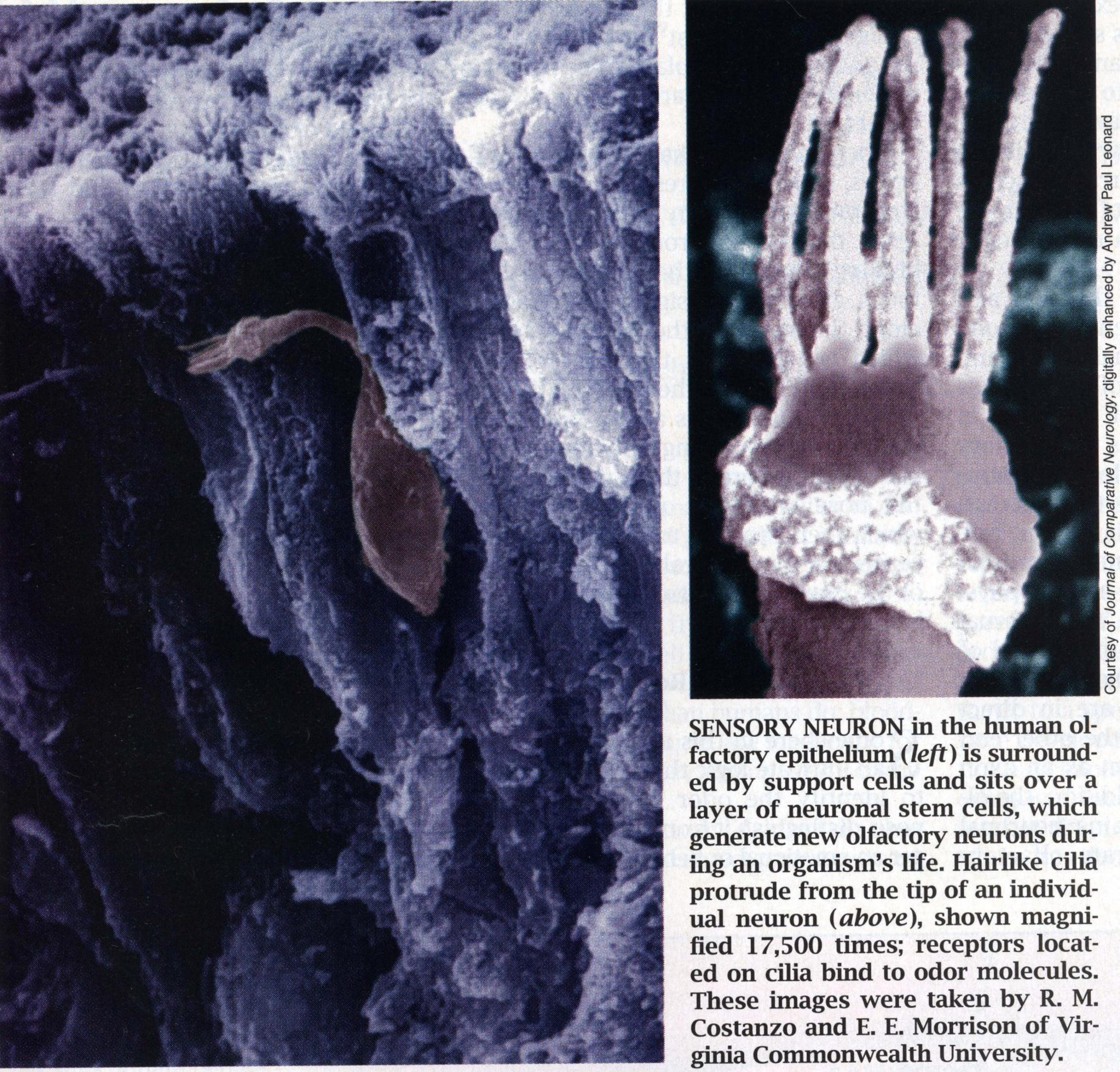
Dendrites of olfactory receptor cells extend into the mucus coating of the epithelium; odorant molecules bind to receptors on the dendrites. Axons of the olfactory receptor cells enter the brain and synapse on cells in the olfactory bulb.



Nasal epithelium

Olfactory sensory neurons

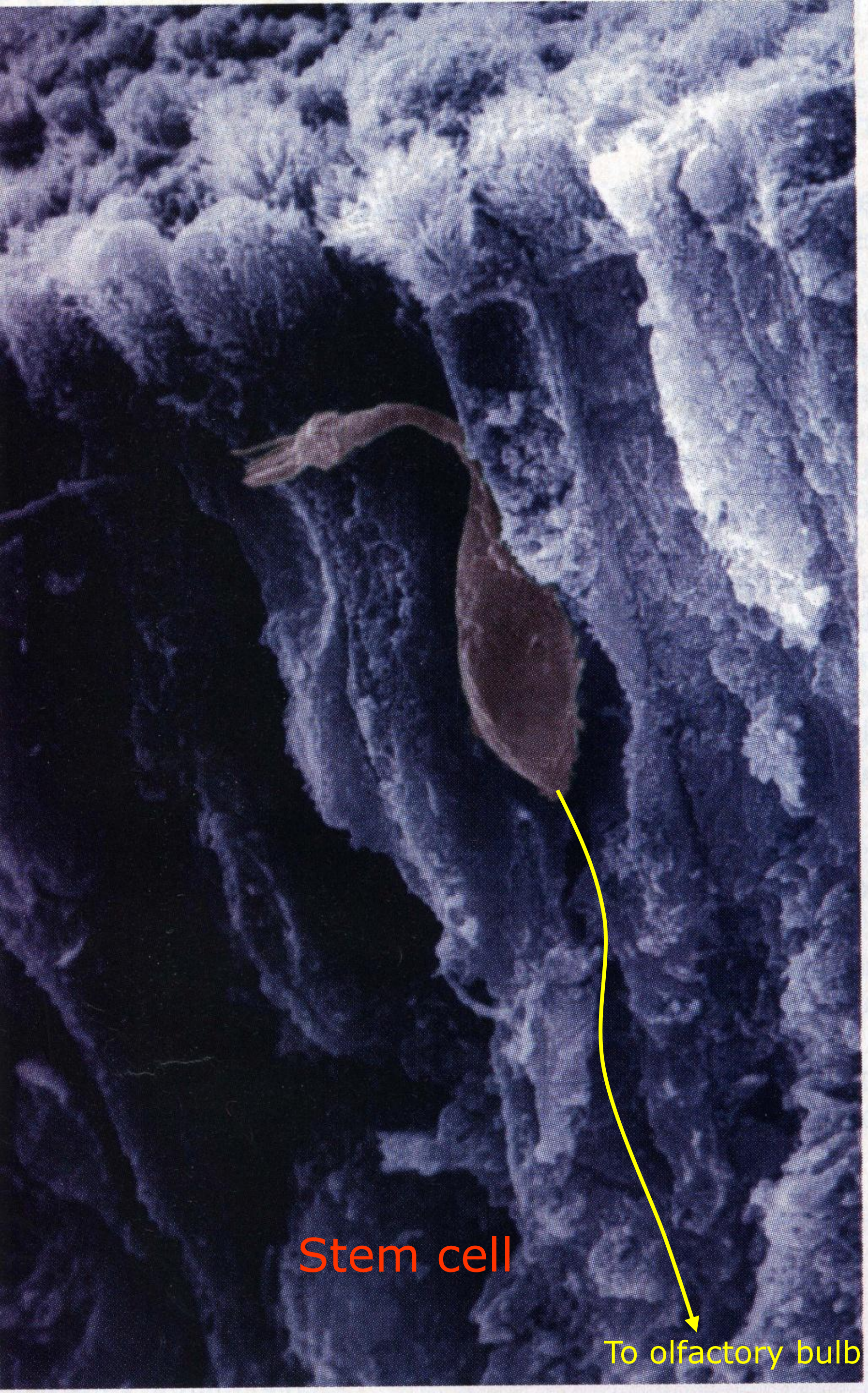
There are about 10 million receptors per side in humans

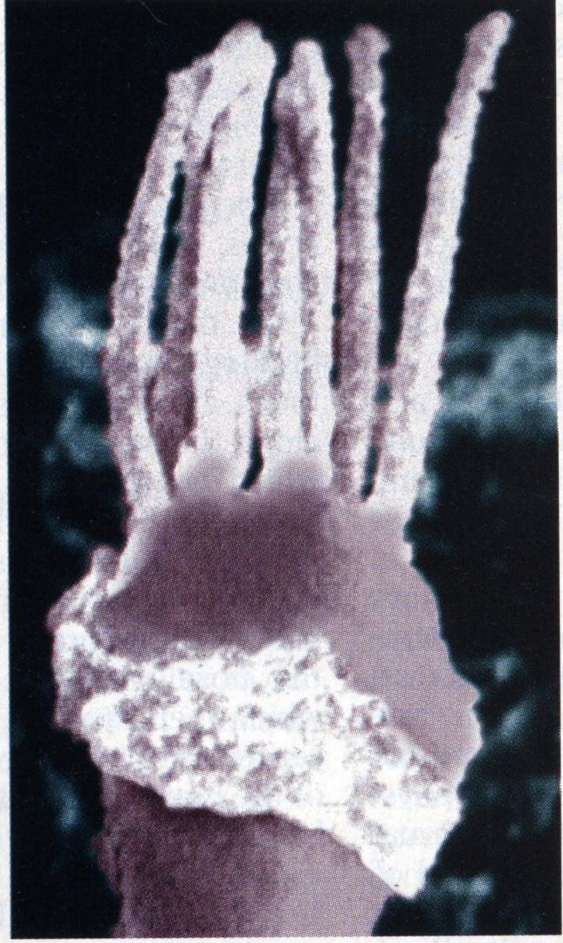


Courtesy of *Journal of Comparative Neurology;* digitally enhanced by Andrew Paul Leonard

SENSORY NEURON in the human olfactory epithelium (*left*) is surrounded by support cells and sits over a layer of neuronal stem cells, which generate new olfactory neurons during an organism's life. Hairlike cilia protrude from the tip of an individual neuron (*above*), shown magnified 17,500 times; receptors located on cilia bind to odor molecules. These images were taken by R. M. Costanzo and E. E. Morrison of Virginia Commonwealth University.

Olfactory sensory neurons





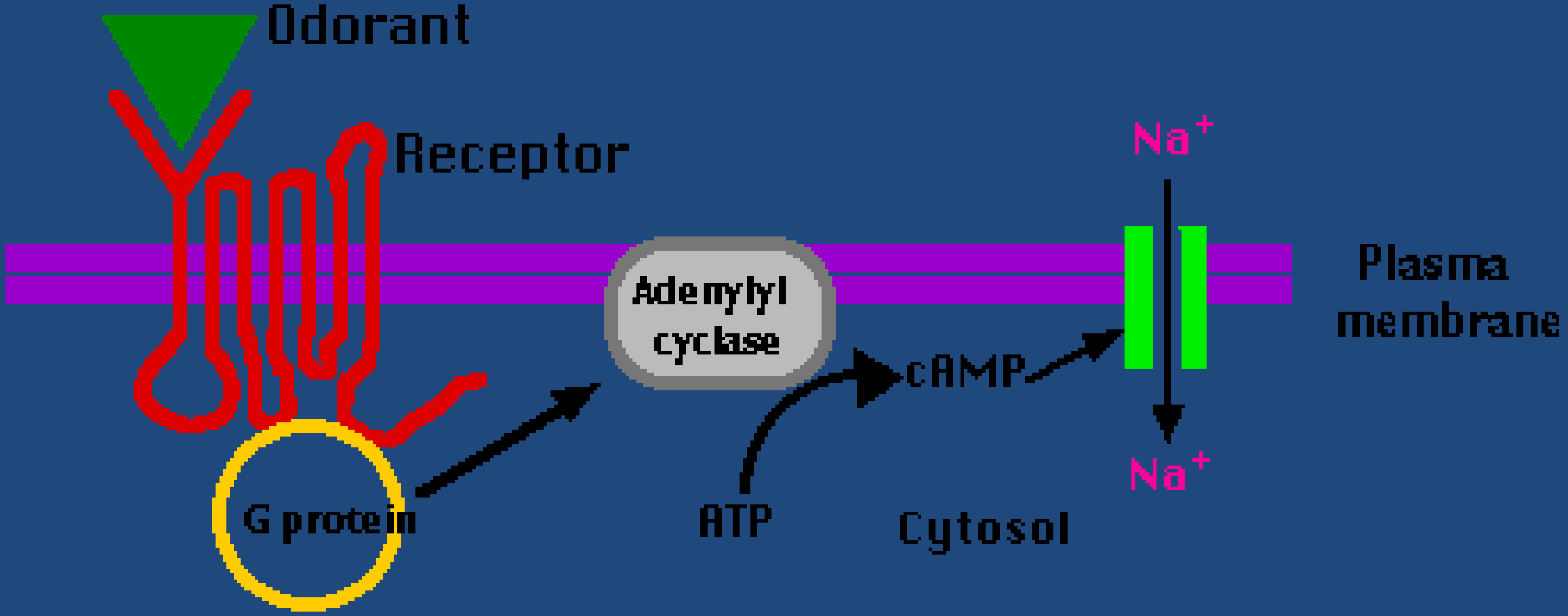
Courtesy of *Journal of Comparative Neurology*; digitally enhanced by Andrew Paul Leonard

SENSORY NEURON in the human olfactory epithelium (*left*) is surrounded by support cells and sits over a layer of neuronal stem cells, which generate new olfactory neurons during an organism's life. Hairlike cilia protrude from the tip of an individual neuron (*above*), shown magnified 17,500 times; receptors located on cilia bind to odor molecules. These images were taken by R. M. Costanzo and E. E. Morrison of Virginia Commonwealth University.

No circuitry or synapses in the epithelium; receptors have axons (thin, unmyelinated, slow) which project directly to the brain.

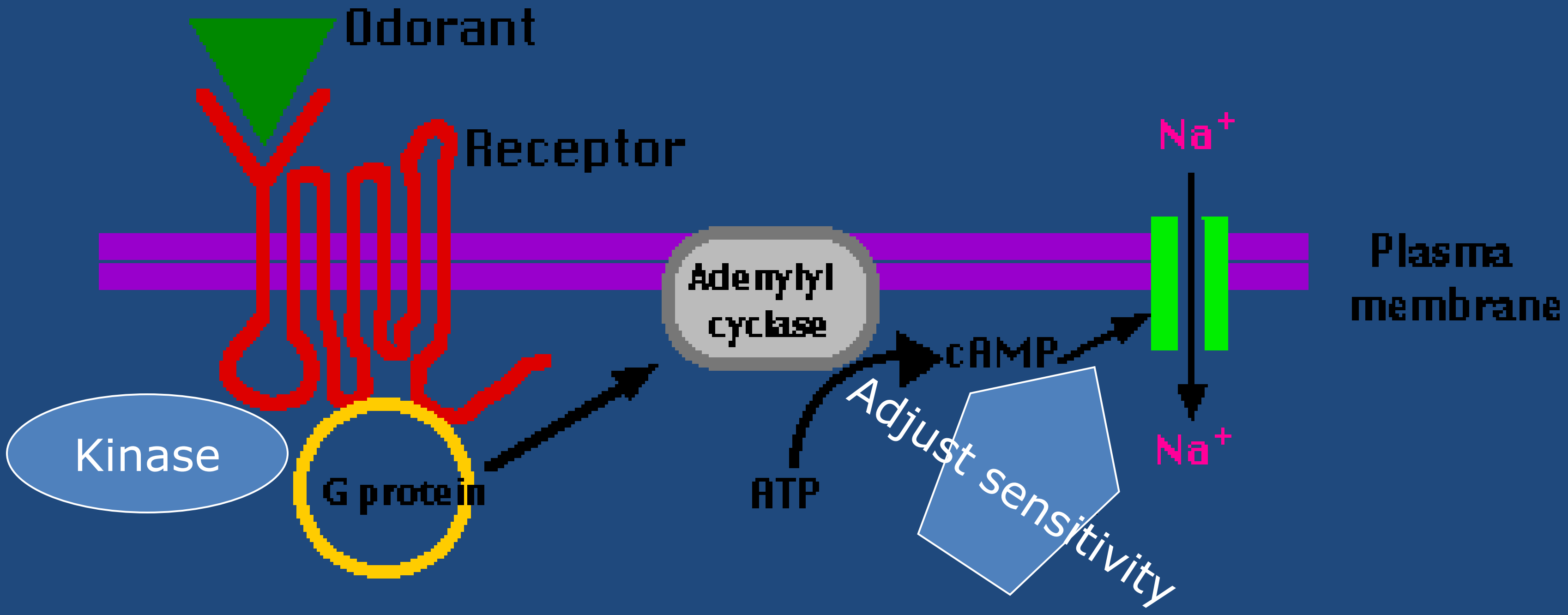
Receptors die and are replaced about every 60 days.

Olfactory receptors use a G-protein coupled transduction mechanism similar to visual receptors



http://users.rcn.com/jkimball.ma.ultranet/BiologyPages/O/Olfaction.html

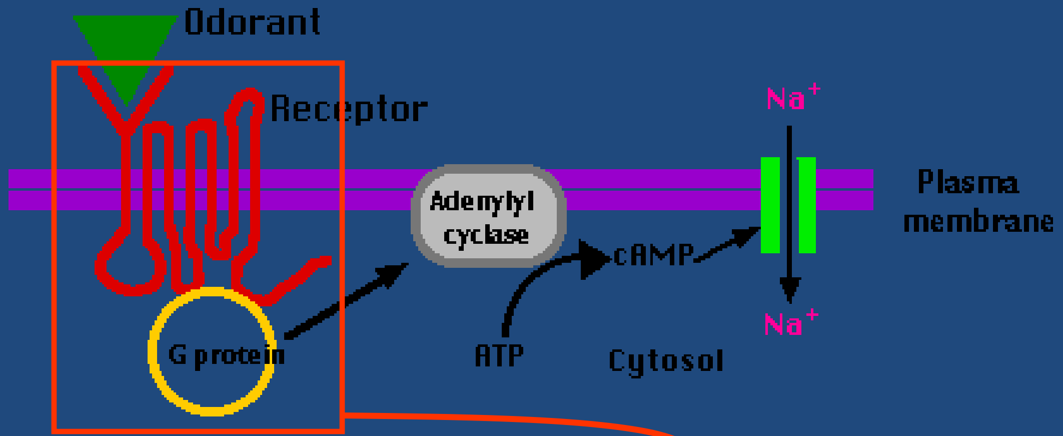
Olfactory receptors show strong adaptation



Mechanisms: 1. Kinase phosphorolation of receptor protein (desensitization to odorant molecules); 2. Adjustment of channel sensitivity to cAMP (up or down depending on odorant concentration)

http://users.rcn.com/jkimball.ma.ultranet/BiologyPages/O/Olfaction.html

Richard Axel and Linda Buck used molecular techniques to determine **the number of different olfactory receptor types**. The concept and strategy:



1. SPECIFICITY WOULD BE BASED ON STRUCTURE OF RECEPTOR-G PROTEIN COMPLEX; THEREFORE, IF YOU DETERMINE THE NUMBER OF DIFFERENT RECEPTOR STRUCTURES, YOU KNOW THE NUMBER OF DIFFERENT FUNCTIONAL TYPES, AND THEREFORE THE NUMBER OF DIFFERENT "PRIME ODORS"

2. STRUCTURALLY DIFFERENT RECEPTOR PROTEINS WOULD BE CODED BY DIFFERENT GENES; CLONE, SEQUENCE, CHARACTERIZE GENES EXPRESSED IN THE OLFACTORY EPITHELIUM, LOOK FOR SYSTEMATIC VARIATION ON G-PROTEIN TYPES

3. LOCALIZE THE EXPRESSED GENES BACK TO THE OLFACTORY RECEPTOR CELLS

Result:
There are **1000 different genes in 4 families**; each codes 7-transmembrane domain G-protein coupled receptor protein that is expressed in olfactory receptors in mice

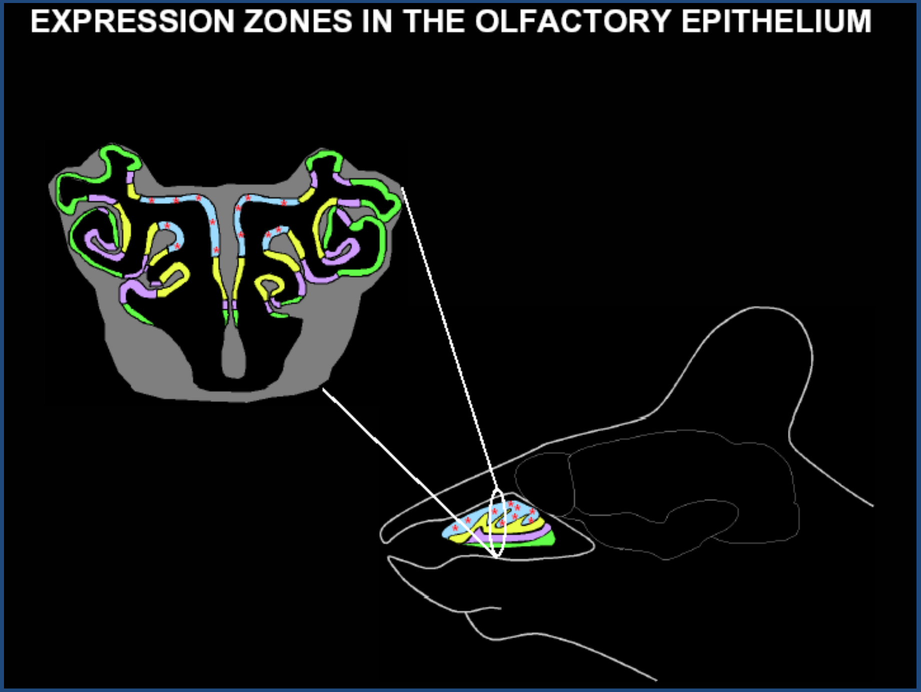
About 350 of these are functional genes in humans; the rest are present as “pseudogenes”

Each receptor cell in the epithelium expresses only one receptor gene

Therefore, each receptor is best “tuned” to one of 1000 different chemical “types”

What these types are is still not clear, nor is how the code gets turned into a “smell”

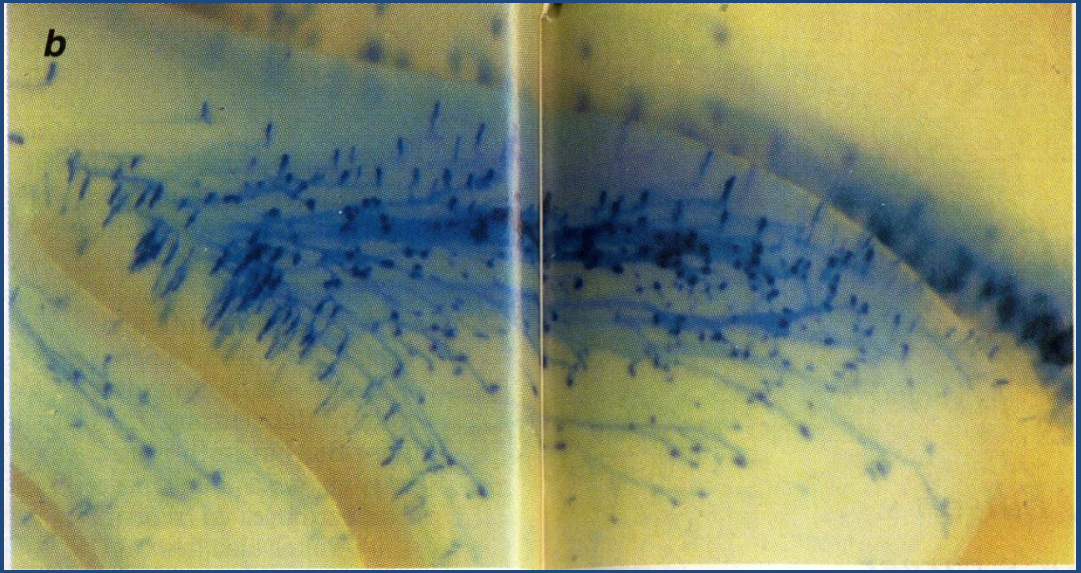
The olfactory epithelium is "mapped", but not in a familiar way

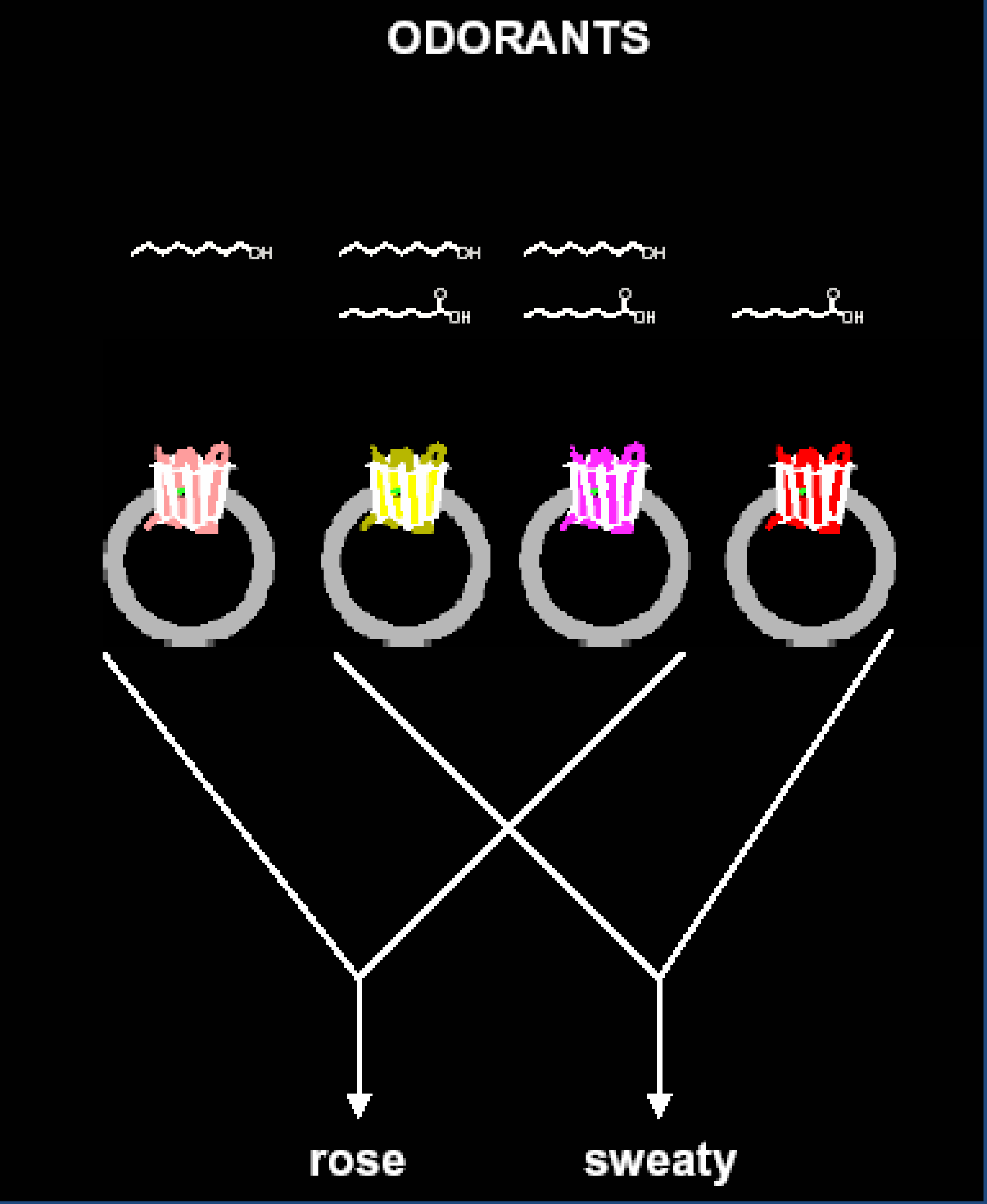


The 4 gene families are expressed in different zones of the epithelium

http://nobelprize.org/medicine/laureates/2004/buck-slides.pdf

Within a zone, different receptor types appear to be randomly scattered



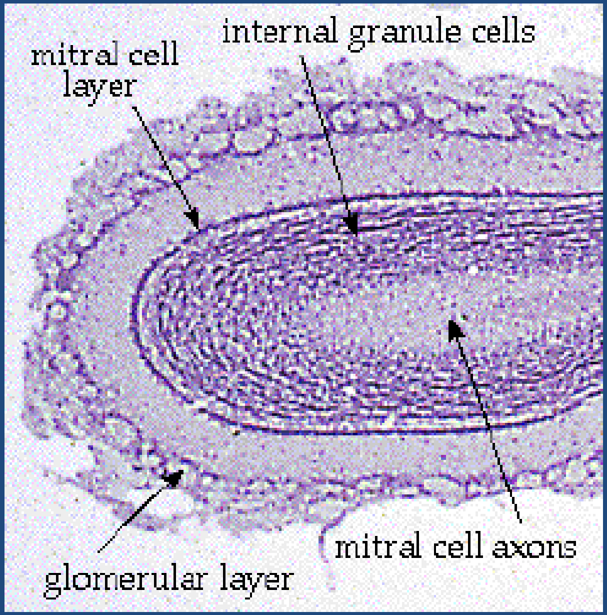


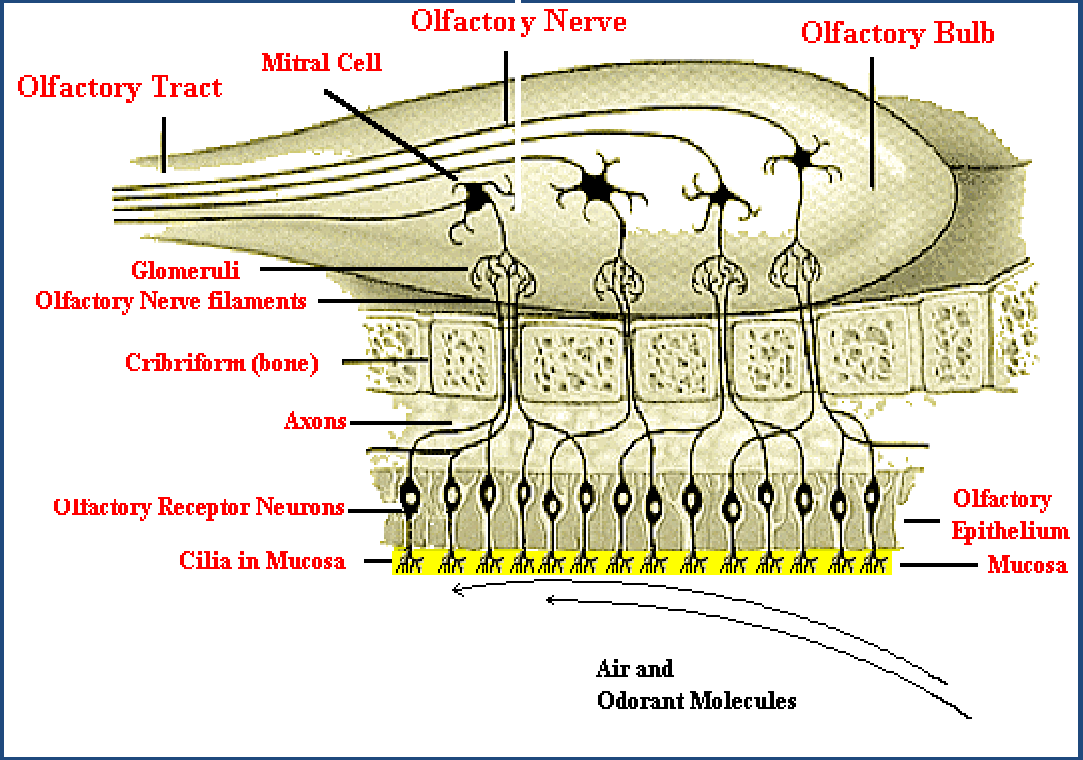
http://nobelprize.org/medicine/laureates/2004/buck-slides.pdf

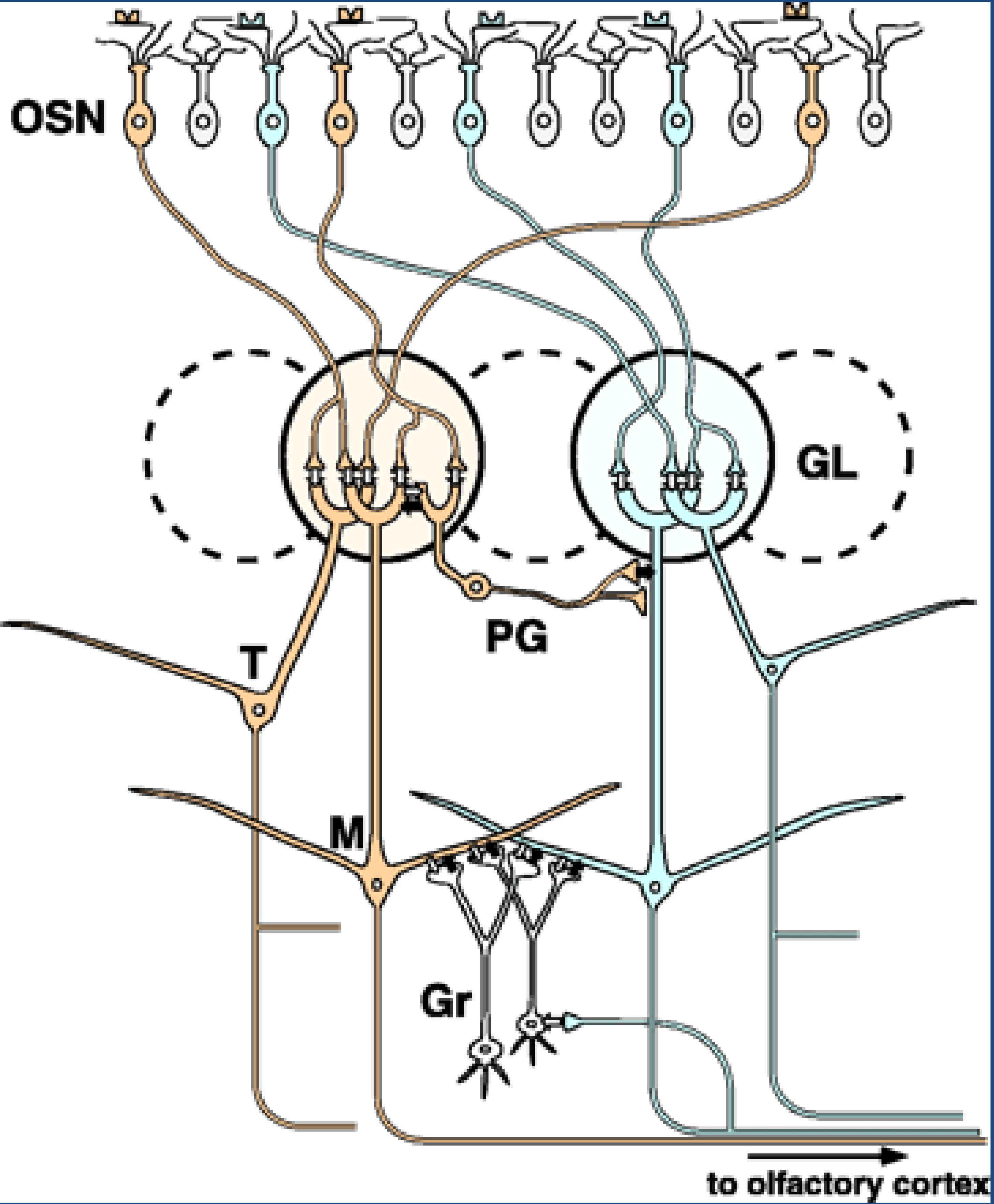
A combinatorial code means that receptors can contribute to the perception of very different smells

Output of the olfactory epithelium goes to the Olfactory Bulb:

Olfactory bulb is a three layered structure. Mitral cells are the principal neurons of the olfactory bulb.

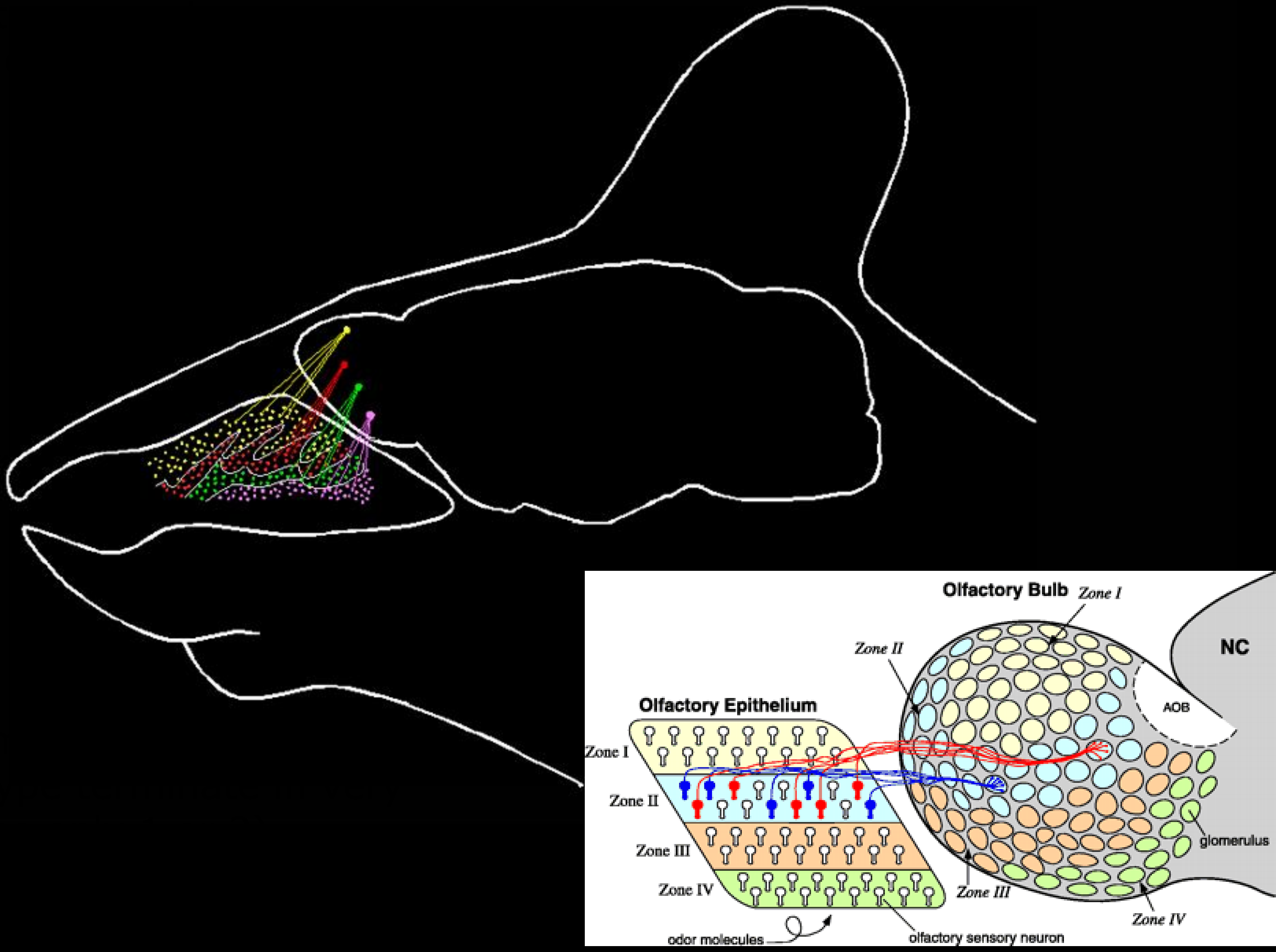






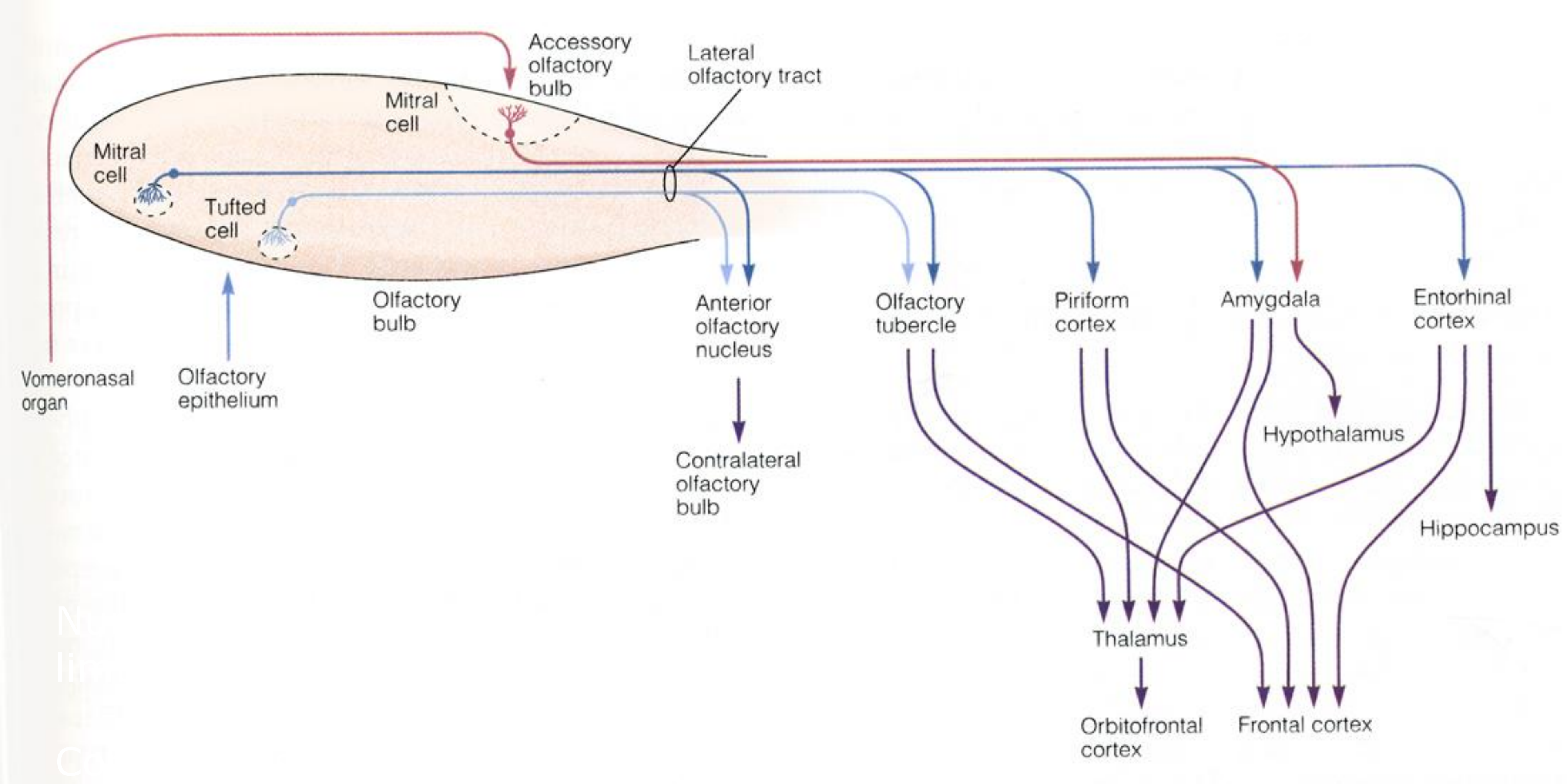
Olfactory Bulb Circuitry: The glomerulus is the basic processing component of the olfactory bulb

Olfactory Bulb Circuitry: Periglomerular cells in the glomerulus and granular cells in the deeper layers mediate local and lateral inhibition


Olfactory Bulb
Zone I
Zone II
NC
AOB
Olfactory Epithelium
Zone I
Zone II
Zone III
Zone IV
glomerulus
Zone III
Zone IV
odor molecules
olfactory sensory neuron

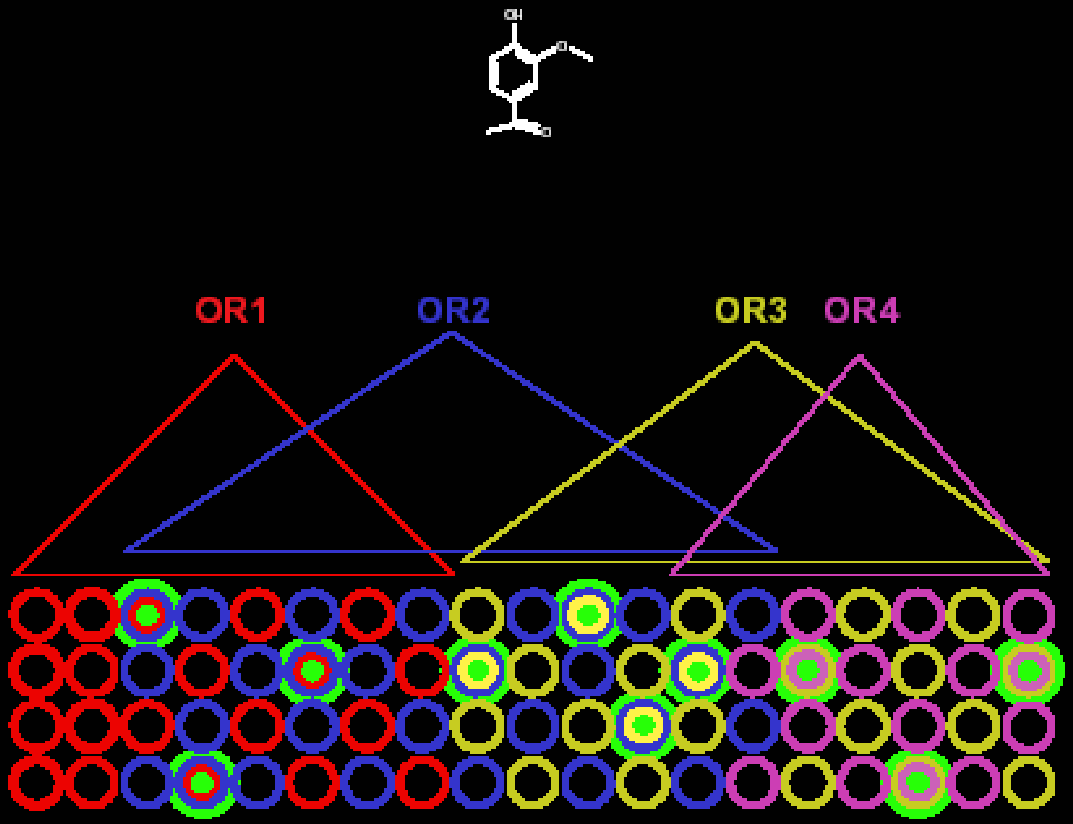
Olfactory pathways out of the bulb are all uncrossed.

The piriform cortex is considered



do not depend on relay through a thalamic nucleus

MODEL: CORTICAL NEURONS AS COINCIDENCE DETECTORS



QUESTION: Why remix inputs after you have gone through all the trouble of separating them out so effectively?

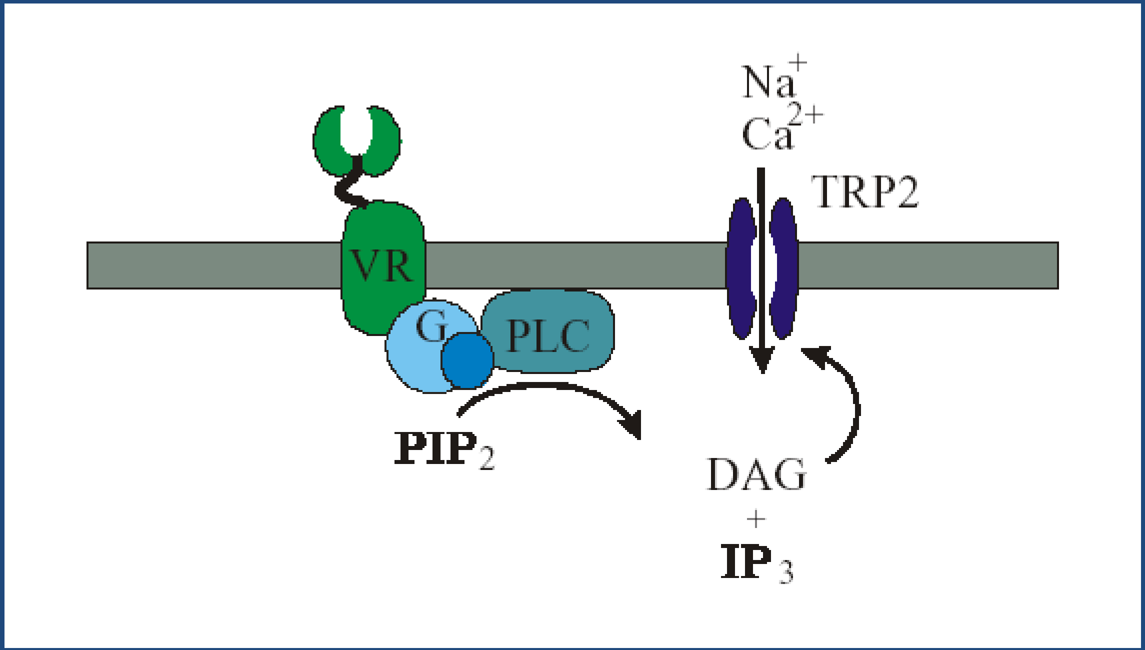
ANSWER: Olfaction may be based on pattern detection: Cortical neurons are concerned with specific combinations of inputs, with each combination corresponding to a percept.

The Vomeronasal System

A second olfactory system is present in most vertebrates. It is separate from the main olfactory system anatomically and functionally.

Vomeronasal receptors are different from main olfactory receptors

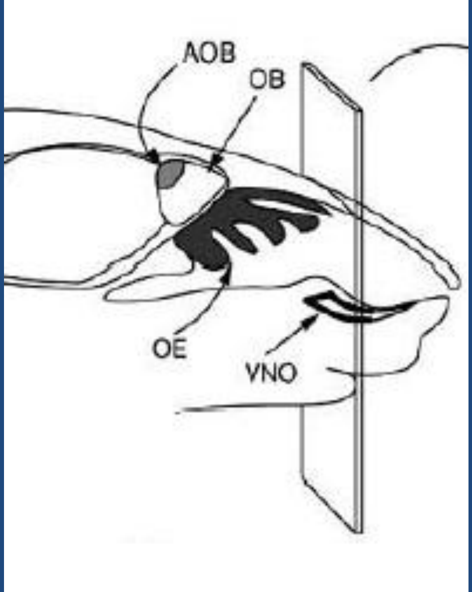
About 100 different receptor types in two gene families; these families are different from the four in which main olfactory receptors are coded



Vomeronasal receptors use a different signal transduction pathway than main olfactory receptors

http://bioweb.usc.edu/courses/2002-fall/documents/neur524-olfactory_transduction.pdf

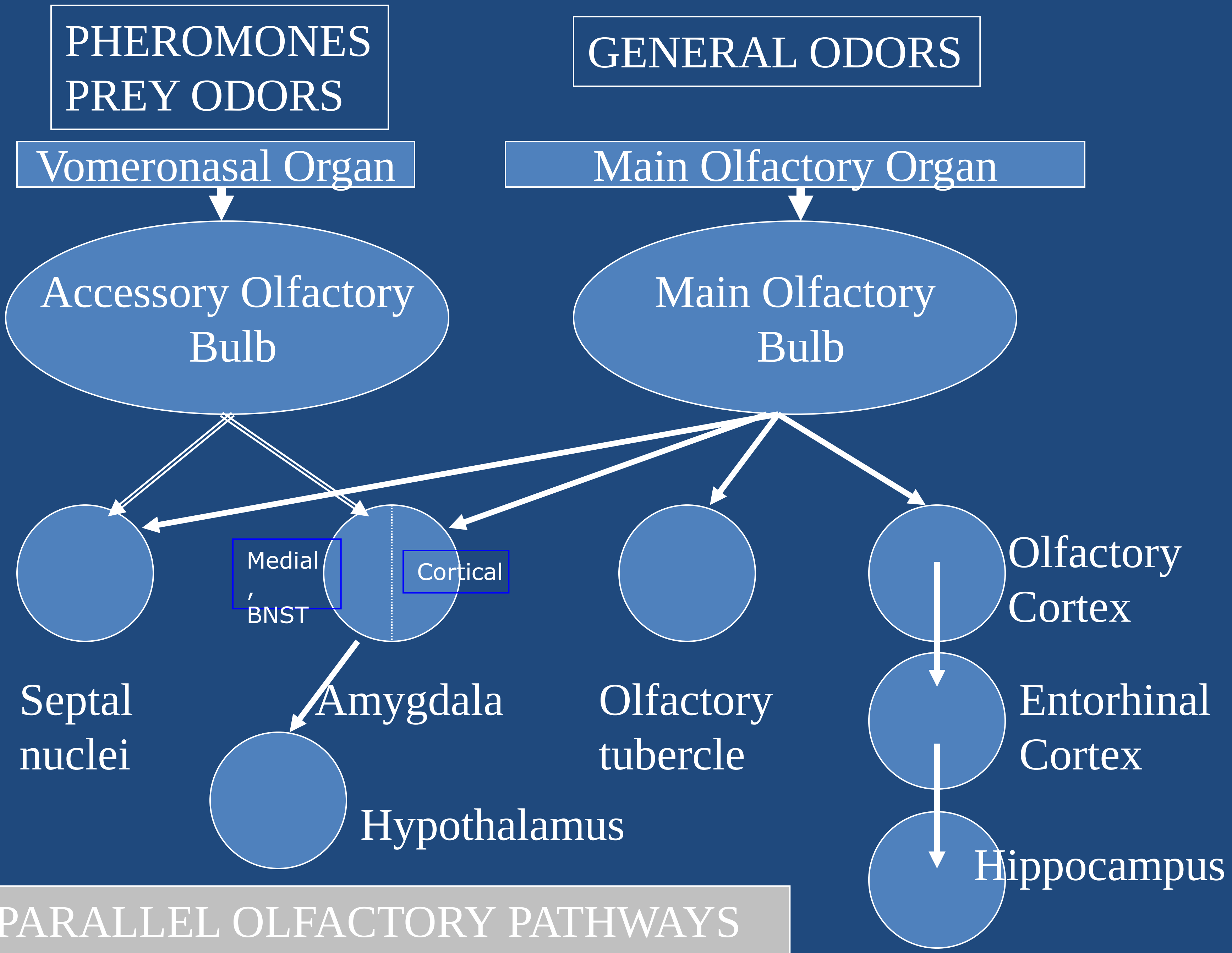
The vomeronasal system is specialized for detecting high molecular weight, relatively nonvolatile chemicals. Its presence is often accompanied by morphological or behavioral specializations for moving such odorants to the vomeronasal epithelium.



LOCATION NEAR NARES, OR OPENING INTO MOUTH CAVITY

VASCULAR "PUMPS"

STEREOTYPED BEHAVIORS: TONGUE FLICKING IN SNAKES "FLEHMEN" RESPONSE IN HORSES



PHEROMONES
PREY ODORS

GENERAL ODORS

Vomeronasal Organ

Main Olfactory Organ

Accessory Olfactory Bulb

Main Olfactory Bulb

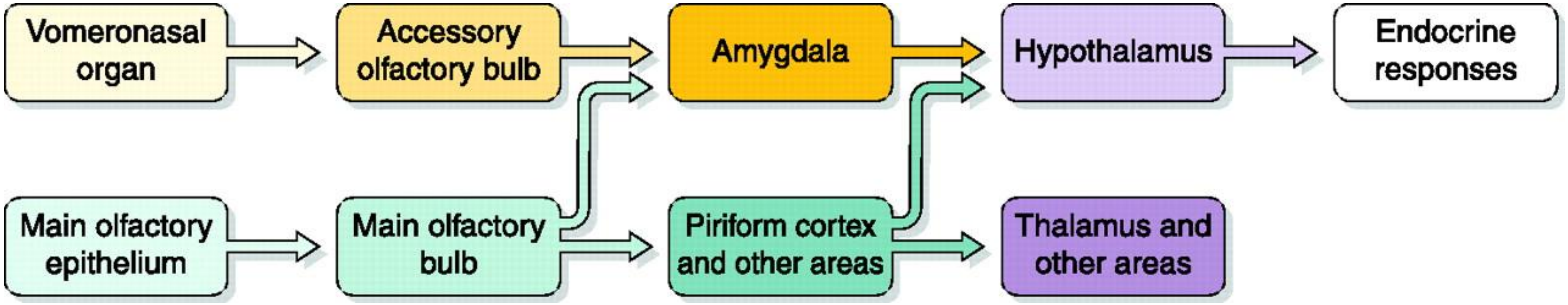
PARALLEL OLFACTORY PATHWAYS

The vomeronasal system is specialized for detecting and processing biologically important odors, especially chemical communication signals (“**pheromones**”)

- Chemical communication is a preeminent social communication channel in most mammals

- Courtship, sexual behavior, aggression, maternal behavior, kin recognition, pair bonding, territoriality, fear and predator avoidance all involve chemical signaling and are controlled by the reception of chemical signals in most mammals

A schematic diagram showing the anatomical pathways of the rodent vomeronasal and main olfactory systems.



Tirindelli R et al. Physiol Rev 2009;89:921-956

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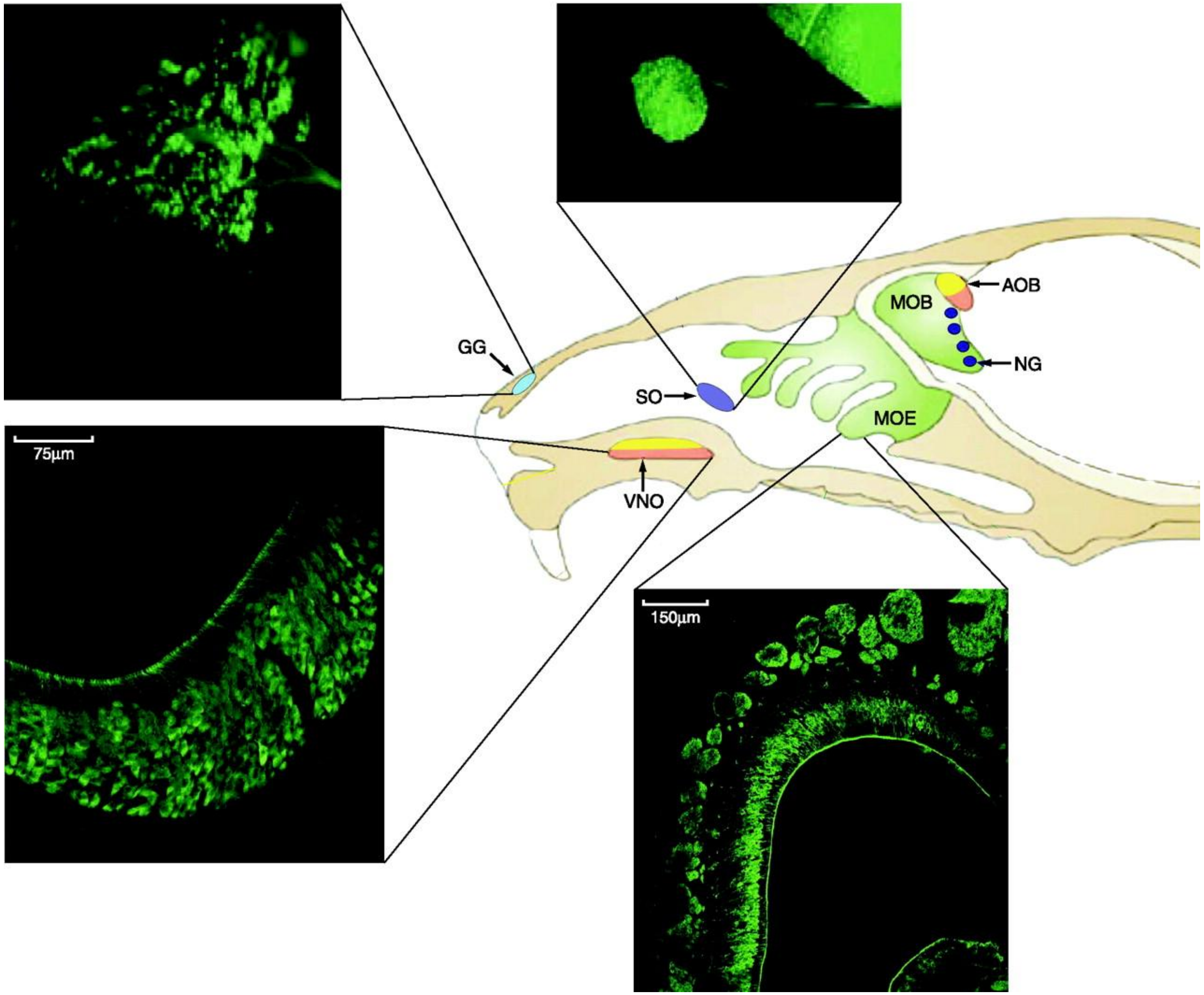
Chemosensory systems in rodents.



Tirindelli R et al. Physiol Rev 2009;89:921-956

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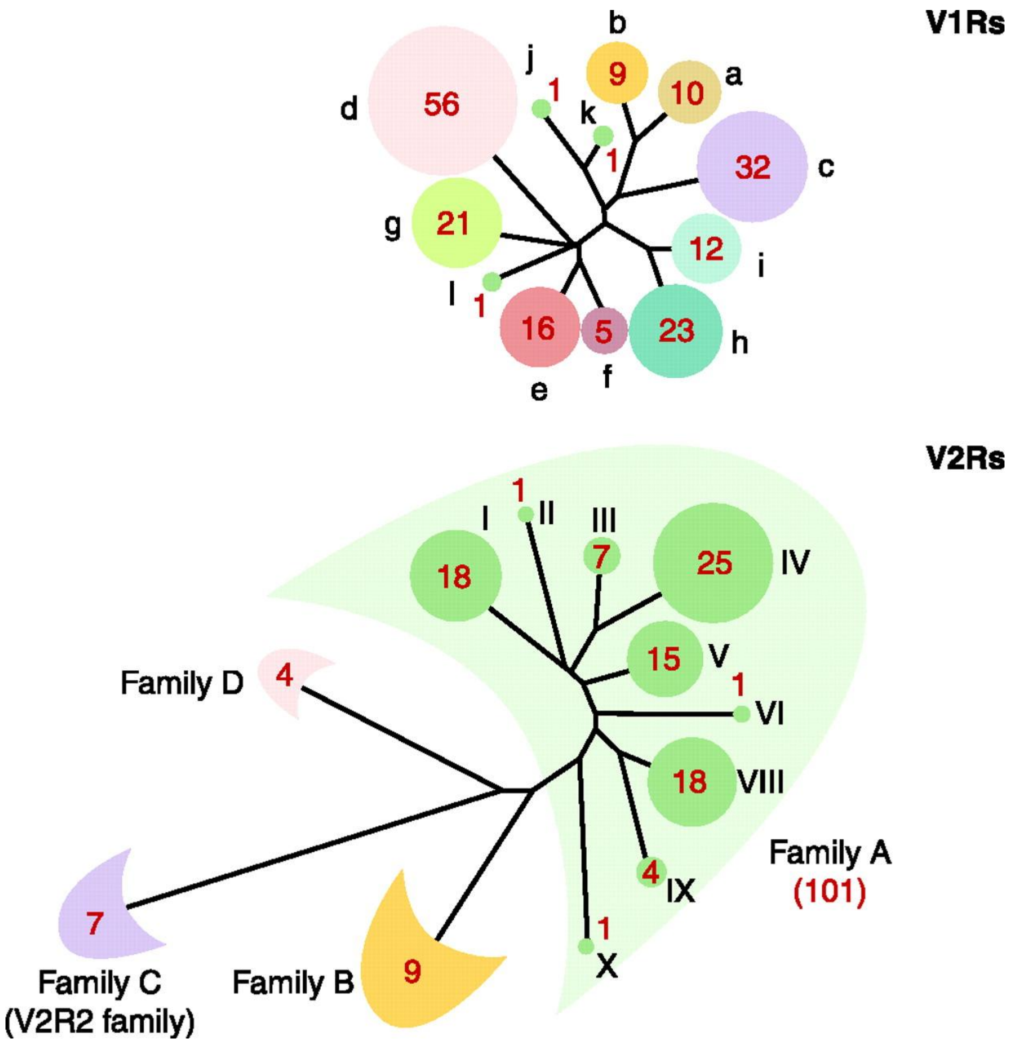
The mouse vomeronasal receptor families.



Tirindelli R et al. Physiol Rev 2009;89:921-956

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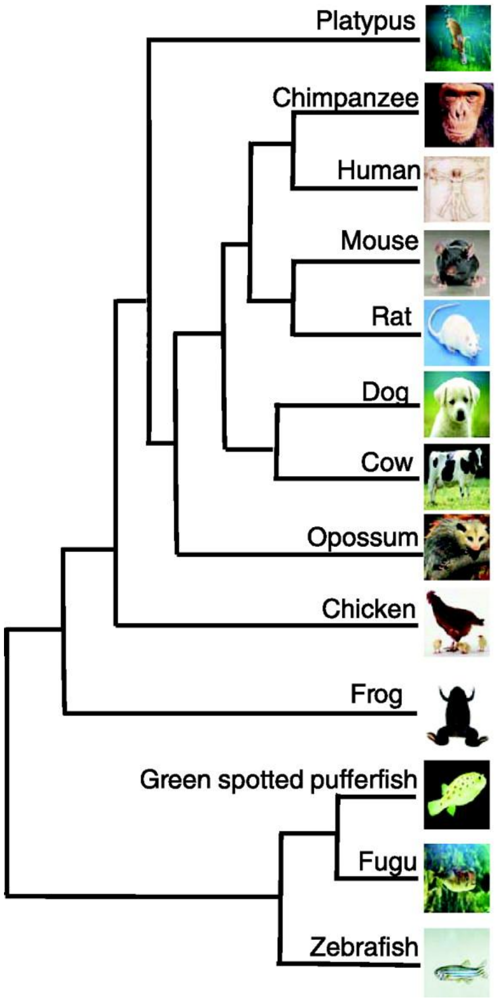
Evolution of nasal chemosensory receptor gene repertoires in vertebrates.



	V1R	V2R	OR	TAAR
Platypus	270(579)	15(112)	261(315)	4(1)
Chimpanzee	0(116)	0(17)	399(414)	3(6)
Human	5(115)	0(20)	388(414)	6(3)
Mouse	187(121)	121(158)	1037(354)	15(1)
Rat	106(66)	79(142)	1201(292)	17(2)
Dog	8(33)	0(9)	876(326)	2(2)
Cow	40(45)	0(16)	970(1159)	17(9)
Opossum	98(30)	86(79)	901(618)	22(0)
Chicken	0(0)	0(0)	82(476)	3(0)
Frog	21(2)	249(448)	410(478)	2(1)
Green spotted pufferfish	1(0)	4(21)	?	?
Fugu	1(0)	18(29)	44(54)	13(6)
Zebrafish	2(0)	44(8)	102(35)	109(110)

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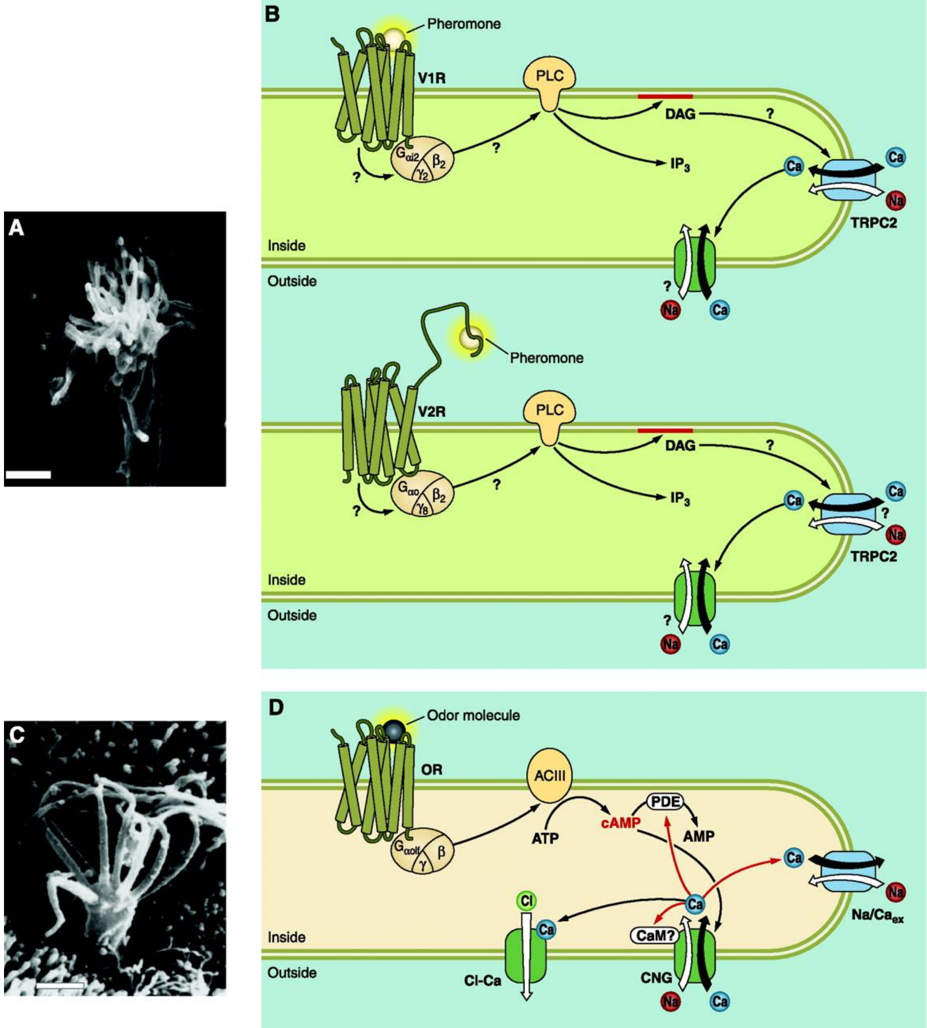
Transduction mechanisms in vomeronasal and olfactory sensory neurons.



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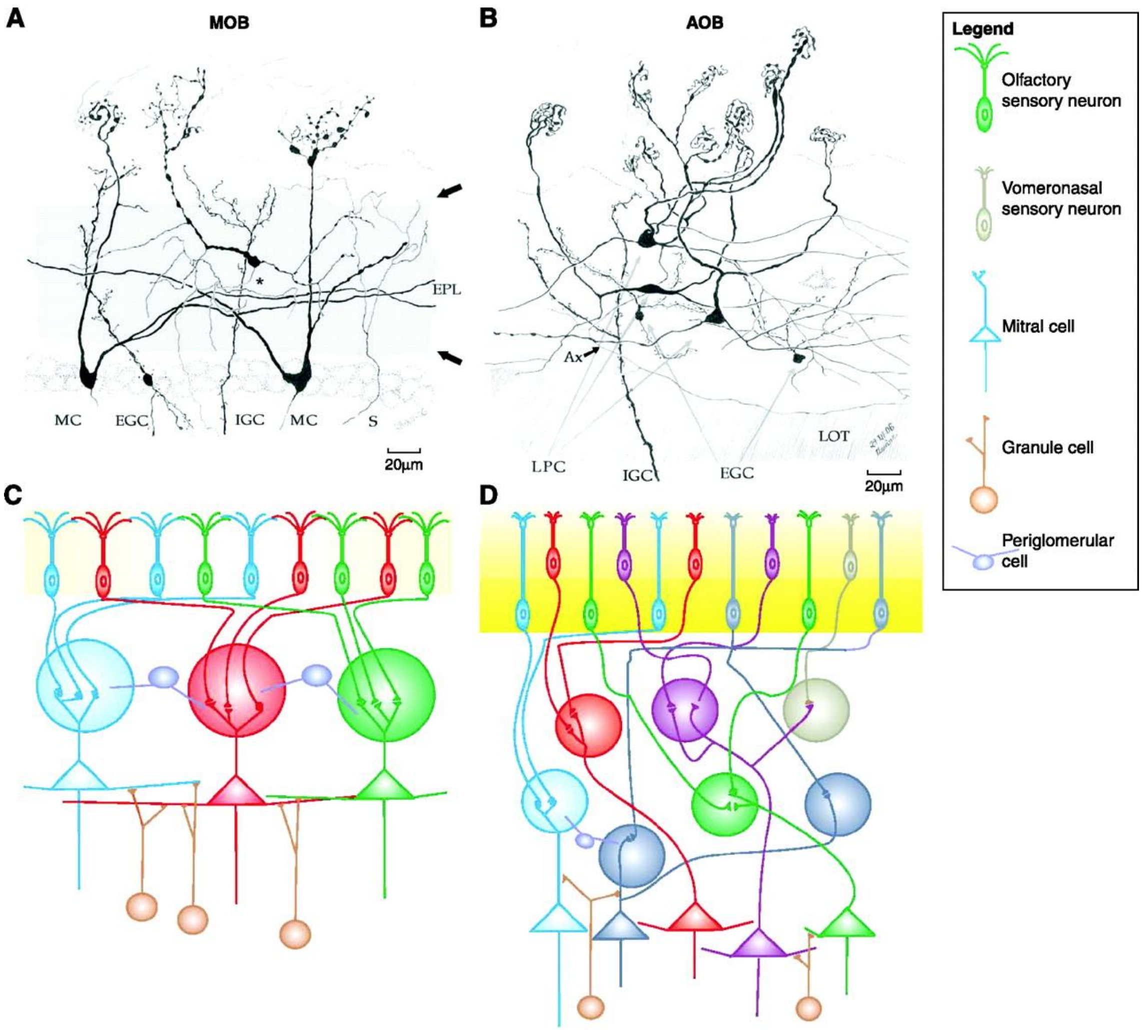
Main and accessory olfactory bulbs.



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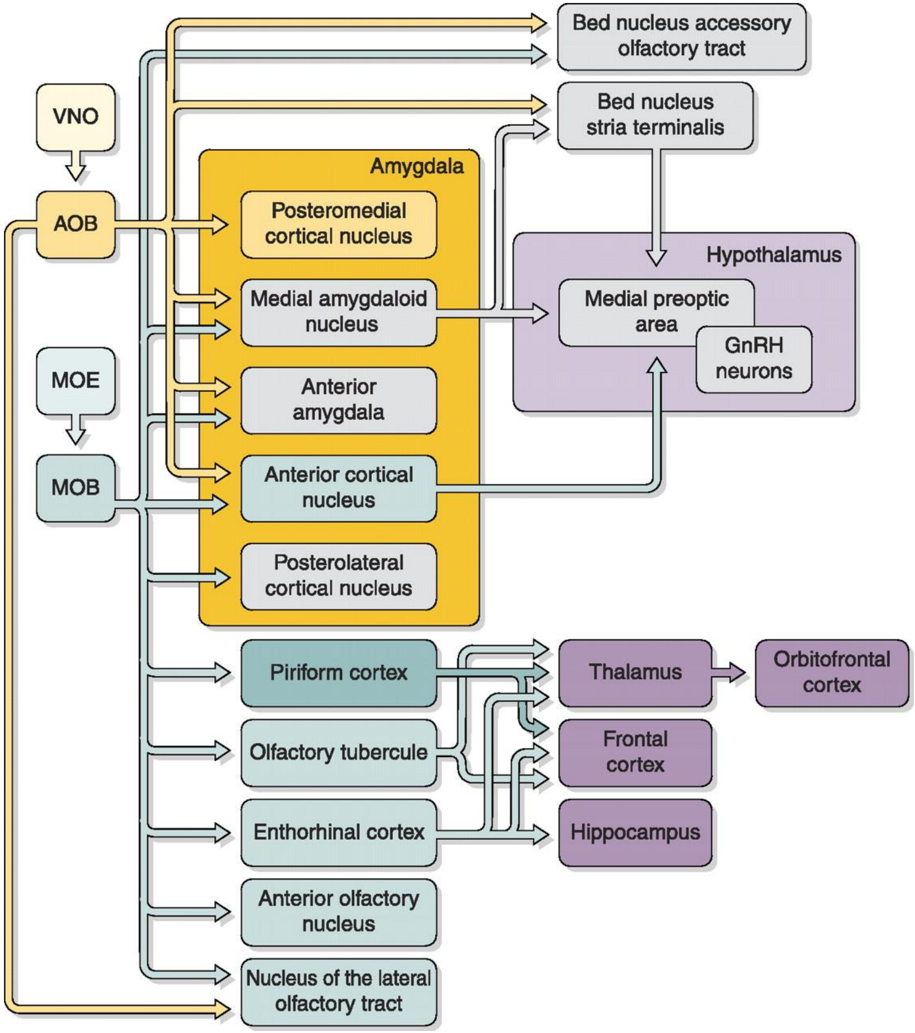
Central pathways involved in processing chemical information by the vomeronasal and main olfactory systems. [Based on data from Martinez-Marcos (229) and Yoon et al.


Bed nucleus accessory olfactory tract
Bed nucleus stria terminalis
VNO
AOB
Amygdala
Posteromedial cortical nucleus
Medial amygdaloid nucleus
Anterior amygdala
Anterior cortical nucleus
Posterolateral cortical nucleus
Hypothalamus
Medial preoptic area
GnRH neurons
MOE
MOB
Piriform cortex
Olfactory tubercule
Enthorhinal cortex
Anterior olfactory nucleus
Nucleus of the lateral olfactory tract
Thalamus
Orbitofrontal cortex
Frontal cortex
Hippocampus

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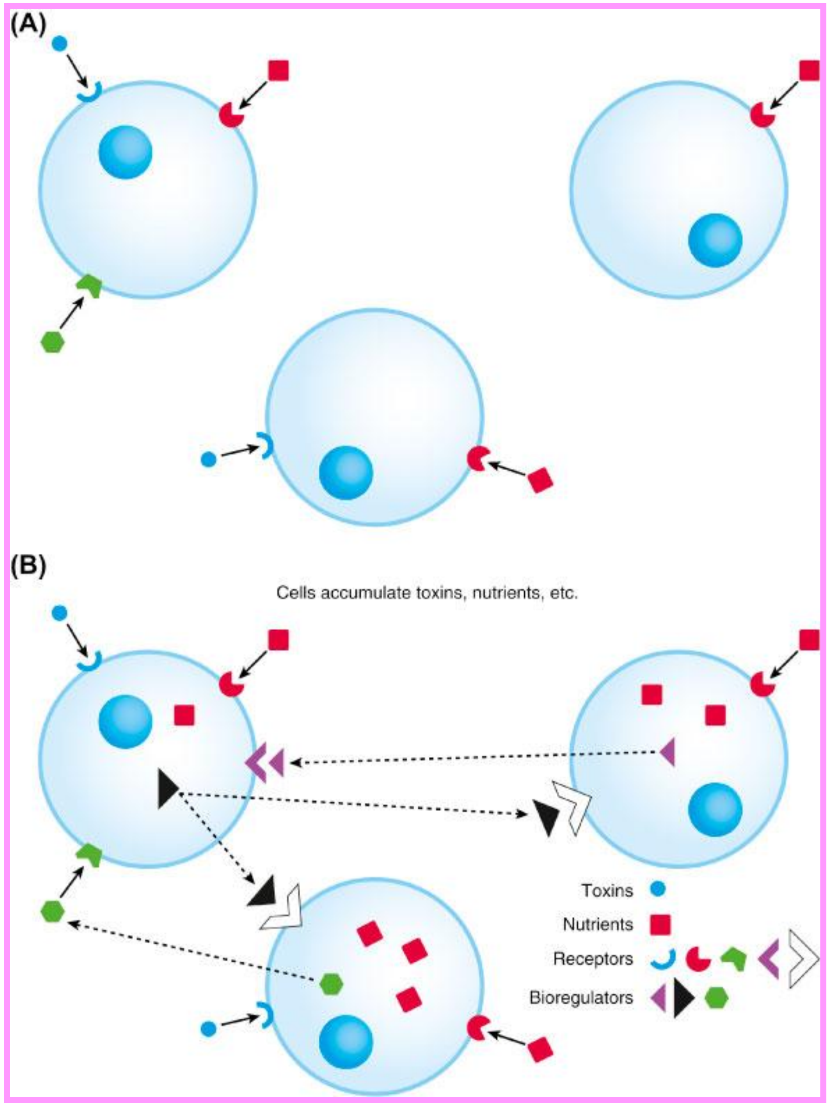
EVOLUTION OF SENSORY SYSTEMS

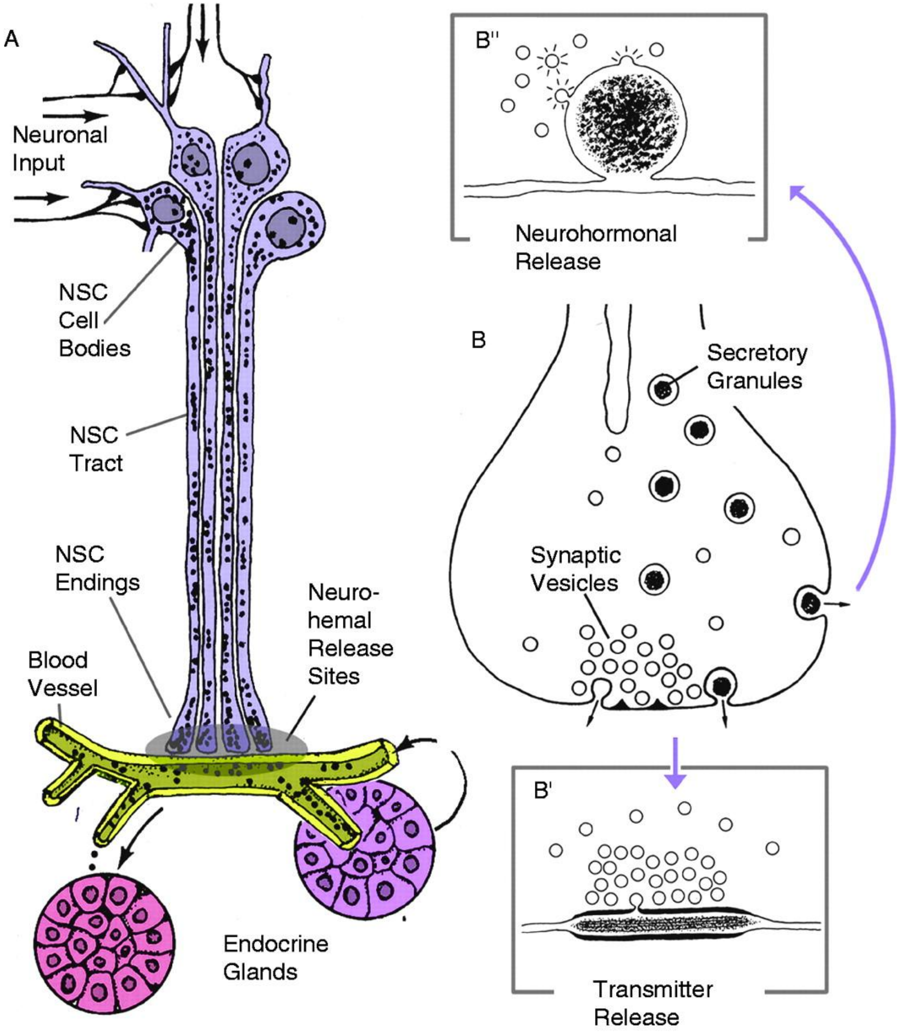
Origins of Chemical Communication



A. Early cells living in the primordial seas developed “receptors” for recognition of water-soluble toxins, nutrients and internal “receptors” for lipids that could readily pass through the membrane. Some of these “receptors” transferred these molecules into the cell for metabolism or detoxification

B. Besides accumulating molecules intracellularly, early cells also released special molecules into the environment that were detected via receptors on other cells and served as a mechanism for cell-to-cell communication. Various features of these ancient mechanisms for accumulation, **detoxification, metabolism, and chemical communication** have persisted in one form or another in all living cells to this day

Figure 1 Structure of the neuroendocrine system.



Hartenstein V J Endocrinol 2006;190:555-570

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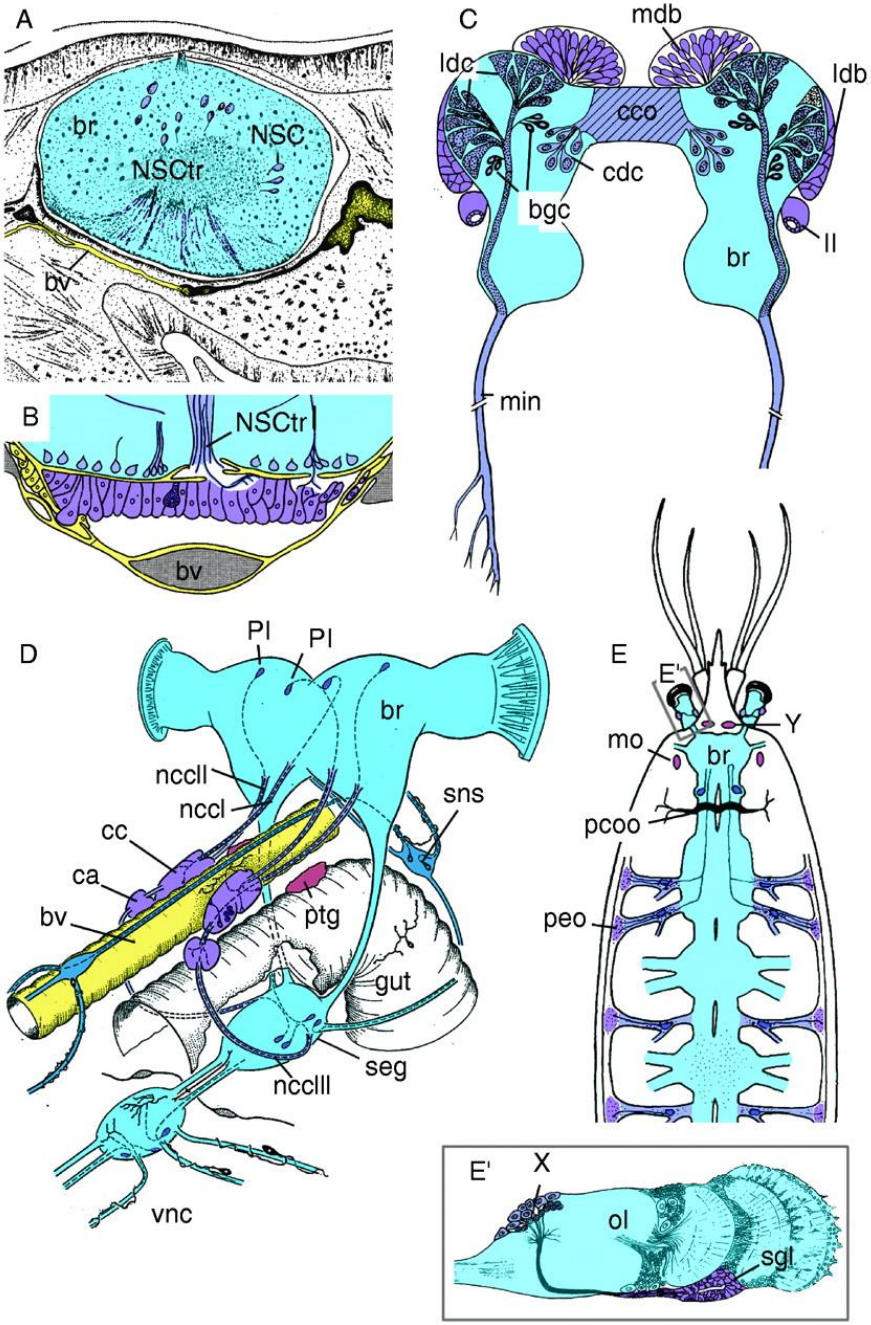
Invertebrate nervous systems clearly illustrate endocrine and nervous system interactions

- Invertebrates have a wide variety of hormones that are involved in the regulation of homeostasis.
  - An example from hydra:
    - One hormone stimulate asexual reproduction.
    - Another hormone prevents sexual reproduction.
  - An example from a mollusk:
    - The hormone that regulates egg laying also inhibits feeding and locomotion.

- Arthropods have extensive endocrine systems regulating molting in insects and crustaceans.
  - The regulation of molting in insects.
    - **Ecdysone** also promotes the development of adult features.
    - Neurosecretory cells in the brain produce **Prothoracicotropic hormone (PTTH)**, which regulates the secretion of ecdysone.
  - **Juvenile hormone (JH)** promotes the retention of larval characteristics.



Comparative overview of important elements of the neuroendocrine system in ((A) and (B)) annelids, (C) mollusks, (D) insects, and ((E) and (E′)) crustaceans.

Hartenstein V J Endocrinol 2006;190:555-570

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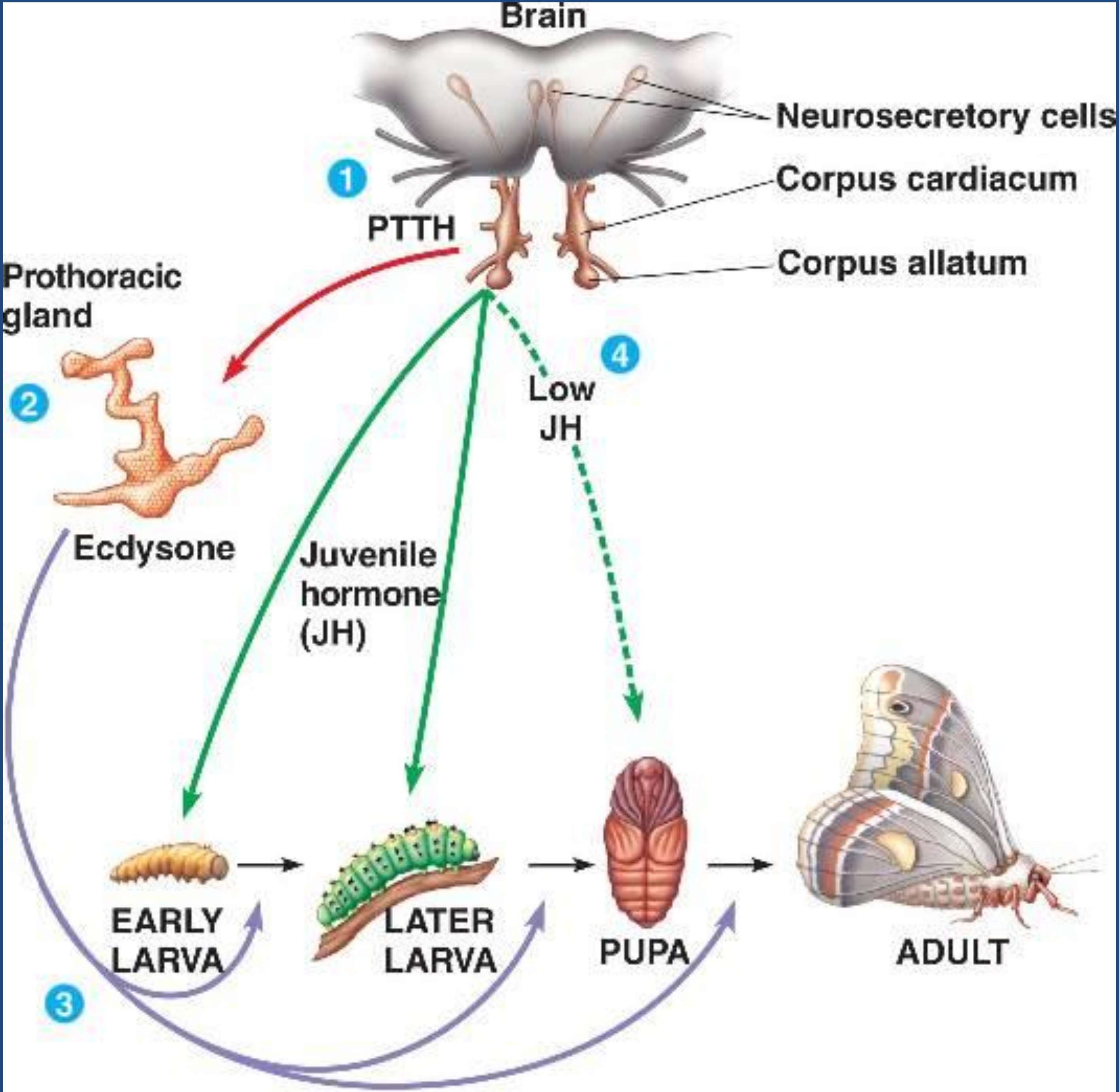
Invertebrate regulatory systems also involve endocrine and nervous system interactions

- Diverse hormones regulate homeostasis in invertebrates
- In insects, molting and development are controlled by three main hormones:
  - Brain hormone stimulates release of ecdysone from the prothoracic glands
  - **Ecdysone** promotes **molting** and **development of adult characteristics**
  - **Juvenile hormone** promotes **retention of larval characteristics**


Brain
Neurosecretory cells
Corpus cardiacum
Corpus allatum
①
PTTH
Prothoracic gland
②
Ecdysone
Juvenile hormone (JH)
④
Low JH
EARLY LARVA
LATER LARVA
PUPA
ADULT
③

Frog Metamorphosis

thyroxin